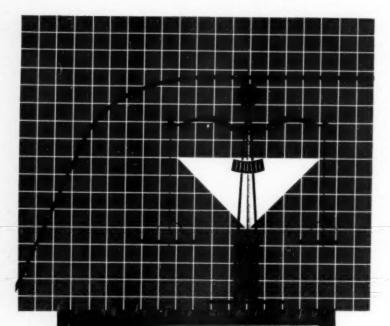
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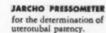




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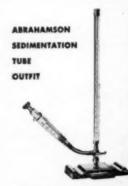






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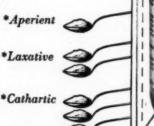
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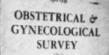
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New Edition of Stedman	Stedman's Medical Dictionary; Edited by Norman B. Taylor, M. D., in collaboration with Allen E. Taylor, M.A.	60
Proctology	Proctology in General Practice; by Comm. (MC) J. P. Nesselrod, USNR	60
Experimental Surgery	Experimental Surgery. Including Surgical Physiology; by J. Markowitz, M.B.E.	62
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"... these statistics are the best that have been reported. In fact, they couldn't be any better."

> Editor: Obstetrical & Gynecological Survey Vol. 4, No. 2: April, 1949; page 190

W. Smith is her article, "Diray, the property of the Prevention and Treatment to mpheations of Pregnancy", in the November, 1948, issue of The American Journal of Obstational Gynecology. This study of 632 pregnancies aboved that, "under stilbestrol treatment the habitual aborter enjoys the same outlook for a living baby as does the average gravida. This is what I mean by saying that these statistics are the best that have been reported".

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Particular Reference to the Use of Dictaylatibestrol.
West. Jr. Surg. Obs. and One 36, 571-603. Nov.
1941. 5. Hamblen, E. C. andocrinsley of Woman,
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-Continued on page 40a



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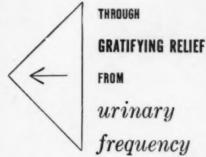


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> Ziporyn, M.; M. Times, New York : 78:205, 1950.

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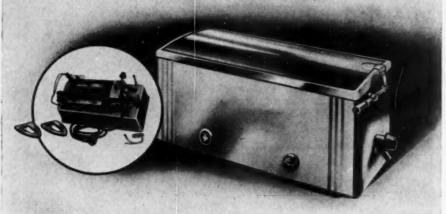
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23a

The physician knows

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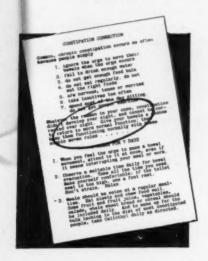
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The "improper habits of living and eating" which cause constipation are not formed overnight. Once deeply ingrained, such habits are not easily changed — and constipation becomes more difficult to correct.

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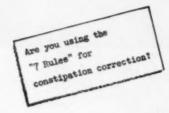
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- 1. Bargen, J. A.: Gastroenterology 13:275, 1949.
- 2. Musick, V. H.: J. Oklahoma M. A. 43:360, 1950.
- 3. Schweig, K.: New York State 5. 1. Med. 48:1822, 1948.
- Council on Pharmacy and Chemistry;
 J.A.M.A. 143:897, 1950.

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 ACTIVE CONSTITUENTS: An aqueous suspension of proceine penicillin G for intramuscular
- injection.

 DOSAGE: One cc. (300,000 units) provides therapeutic levels for at least 24 hours. I cc. (300,000 units) every 24 hours ample for most infections. For overwhelming infections; I cc. injections every 12 hours or 2 cc. injections daily.
- HOW SUPPLIED: I cc. vial—300,000 units; 5 cc. vials—1,500,000 units; 10 cc. vials—3,000,000 units; vial with disposable cartridge syringe (300,000 units).

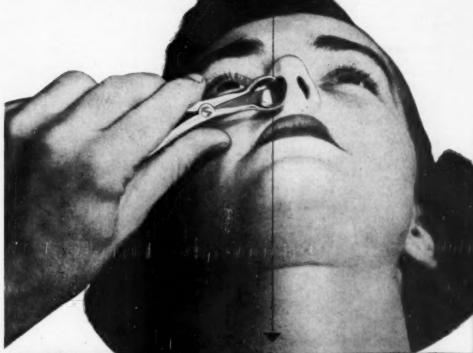
Topaminic

1-51

- MANUFACTURER: Sharp and Dohme, Philadelphia 1, Pa.
- INDICATIONS: For prompt relief from acute itching due to atopic and contact dermatitis and a variety of other allergic skin disorders.
- ACTIVE CONSTITUENTS: Methapyrilene hydrochloride, potent antihistamine effective in alleviating many irritive skin conditions such as eczema, urticaria, angioneurotic edema, and dermographia, Topaminic combines the protective quality of calamine with the anesthetic effect of benzocaine and the antiseptic property of hexylated m-cresol in a bland water-washable base.
- DOSAGE: Applied topically three or four times daily, according to clinical judgment. A light gauze bandage may be used if desired.
- HOW SUPPLIED: In I oz. tubes.

-Continued on page 30a

cleared...



Privine

Ciba

Artisone Acetate

1-51

MANUFACTURER: Wyeth, Inc., 1600 Arch St., Philadelphia 3, Pa. INDICATIONS: To alleviate the local effects of rheumatoid arthritis.

ACTIVE CONSTITUENTS: Prebediolone Acetate or 21 acetoxy-pregnenolone.

DOSAGE: As indicated.

HOW SUPPLIED: In 10 cc. ampules containing 100 mg. per cubic centimeter.

Synthenate Tartrate

MANUFACTURER: George A. Breon & Company, 1450 Broadway, New York 18, New York. INDICATIONS: An effective aid against the common cold. Also found useful in treatment during convalescence in chronic exhaustive conditions and to support peripheral circulation in most hypotensive states.

ACTIVE CONSTITUENTS: Each cc. contains p-methyl-aminoethanolphenol tartrate 0.1 Gm. DOSAGE: As indicated.

HOW SUPPLIED: In 1 cc. ampuls in boxes of 12's and 25's.

Parbrom

1-51

MANUFACTURER: Central Pharmacal Company, Seymour, Indiana.

INDICATIONS: Secures complete or partial relief of premenstrual headache, breast tenderness, irritability, abdominal distention, etc. in a majority of cases; patients are enabled to perform their daily activities without incapacitation or distress. Provides symptomatic relief in patients whose weight gain during the premenstrual period is reduced by administration of the medication. Hence, it is believed that the drug directly or indirectly attacks the tissue edema occurring in these patients.

ACTIVE CONSTITUENTS: Pyranisamine bromotheophyllinate.

DOSAGE: As indicated.

HOW SUPPLIED: In bottles of 100 and 500 tablets, each containing 50 mg. of Pyrabrom.

Sucaryl Sodium Sweetening Solution

MANUFACTURER: Abbott Laboratories, North Chicago, Illinois.

INDICATIONS: For sweetening foods for diabetic, reducing and other sugar-restricted diets.

Unlike saccharin, it can be used in cooking, baking and canning without loss of sweetness, and when used in ordinary quantities does not leave a bitter or metallic after-taste. The liquid form blends readily with most recipe ingredients and eliminates the dissolving time of tablets in iced drinks.

ACTIVE CONSTITUENTS: Cyclamate sodium.

DOSAGE: Each 15 minins (1/4 teaspoonful) is equivalent in sweetening power to approximately two teaspoonfuls of sugar or two Sucaryl tablets. A spout on the bottle cap enables the user to drop or sprinkle a small quantity on cereals, fruit or other foods. The entire cap may be removed for pouring the solution into a spoon or measuring glass. Until further experience has been accumulated, it is recommended that adults limit daily intake to about 11/2 teaspoonfuls of the solution per day.

HOW SUPPLIED: In 4 fl.-oz. bottles, singly and in packages of 12.

My-B-Den Sustained-Action

1-51

MANUFACTURER: Ernst Biscoff Company, Inc., Ivoryton, Connecticut.

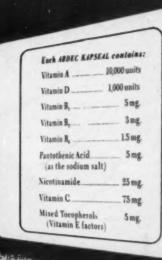
INDICATIONS: In treatment of ulcers, stasis dermatitis and pruritus accompanying varicose veins and chronic venous insufficiency. Complete subsidence or marked amelioration of symptoms has been obtained in pruritus ani, vulvae, and scroti, postpartum pruritus, idiopathic pruritus, and pruritus associated with jaundice, Hodgkin's disease, diabetes mellitus, and penicillin reaction.

ACTIVE CONSTITUENTS: By slow release of its active agent, sustained-action MY-B-DEN acts for 24 to 48 hours, maintaining therapeutic blood levels of ATP, a potent vascdilator and essential intermediary link in basic life processes. My-B-DEN has been shown

so far to be completely non-toxic in dosage many times the therepeutic dose.

DOSAGE: A single injection of this long-acting form of adenosine-5-monophosphate takes the place of five.

HOW SUPPLIED: In 10 cc. multiple dose vials, sufficient for a course of treatment.



When prescribing a preparation for prevention or treatment of vitamin deficiencies, label content is required reading. Clinical experience has shown that vitamin deficiency states are frequently of multiple origin: obviously, in such instances, a quality multivitamin preparation of suitable potency is indicated.

ABDEC® KAPSEALS®

ABDEC KAPSEALS combine nine important vitamins. Broad coverage provided by these components facilitates prevention and correction of nutritional deficiencies.

For routine prophylaxis, to offset debility following illness or operation, and during pregnancy and lactation, ABDEC KAPSEALS are a dependable nutritional supplement...uniformly potent...and readily accepted by your patients.



DOSAGE: for the average patient one ABDEC KAPSEAL daily; during pregnancy and lactation two KAPSEALS daily. Three KAPSEALS daily are suggested for patients in febrile illness, both for pre-operative and for post-operative patients and for patients in other situations in which vitamin deficiencies are likely to occur, as with treatment with newer antihiotics given orally over periods of seven or more days.

PARKE, DAVIS & COMPANY



AFTER YEARS

Literature and directions for administration of ACTHAR, including contraindications, are available on request.

ACTHAR is supplied in 10, 15, 25, 40 and 50 mg. Yials, in packages of 10 and 25 vials.

hours

Reversal of heretofore intractable diseases beginning within hours after instituting ACTHAR therapy, is the culmination of years of intensive research by The Armour Laboratories, together with independent investigators.

ACTHAR, the first adrenocorticotropic hormone made available to the physician, represents the physiologic stimulus for the adrenals to produce and discharge the complete spectrum of cortical hormones.

Virtual absence of cumulative effects permits precise, yet flexible, dosage schedules. The exclusive utilization of physiologic mechanisms for its powerful therapeutic action furthermore contributes to the clinical safety of ACTHAR.

ESTABLISHED INDICATIONS: Collagen diseases or connective tissue diseases, such as rheumatoid arthritis, rheumatic fever, acute lupus reythematosus; hypersensitivities, such as severe asthma, drug sensitivities, contact dermatitis; most acute inflammatory diseases of the eye; acute inflammatory conditions of the skin, such as acute pemphigus and exfoliative dermatitis; inflammatory conditions of the intestinal mucosa, such as ulcerative colitis; and metabolic diseases, such as acute gouty arthritis and secondary adrenal cortical hypofunction.

ACTHAR

Armour Laboratories Brand of Adrenocorticotropic Hormone (A. C. T. H.)

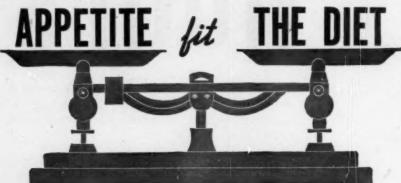


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PHYSIOLOGIC THERAPEUTICS THROUGH BIOCHEMICAL RESEARCH

make



It is well known that the craving for food which besets many obese people cannot easily be controlled by the will alone. For them, adherence to a reducing diet often imposes a nervous strain, with consequent tension and irritability; and if they succumb to their urge to eat more, they have a sense of failure.

But appetite can now be modified by oral administration of 'Methedrine'. Then avoidance of over-eating becomes practically effortless, and the patient feels fitter and cheerful, as well as satisfied . . . with his meals and with his achievement.

Trials have shown that 'Methedrine' is a reliable anorexiant, and that it is effective in low dosage

Literature describing dosage and recommended regimen will be sent on request.

Ray, H. M.: Am. J. Digest. Dis., 14:153, 1947. Shapiro, S.: Ibid, 14:261, 1947.

Methamphetamine Hydrochloride (d-Desoxyephedrine Hydrochloride)

Compressed products of 5 mg.—Scored to facilitate division.



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CHRONIC SUPPURATIVE OTITIS
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FORMULA: Unou 2.0 GRAINS
Substitutional 1.5 GRAINS
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Nasal Decongestant WITHOUT Circulatory or Respiratory Effect

POSTOPERATIVE NASAL SHRINKAGE HAY FEVER
ALLERGIC AND HYPERTROPHIC RHINITIS

FORMULA: Descryephedrine Saccharinate 0.50% w/v in an isotenic aqueous spiraten with 0.02% Laurylammonium saccharin. Florared, pH 6.4.

Supplied to THE DOHONY SPRAY-O-MIZER

PLEASANT - EFFICIENT NON-TOXIC - BACTERICIDAL (Combination Spray and Dropper)
"TRADE MARK—PAT. PEND.
Also for Office and Hespitel uses in Pint battles.

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That's the sign for SYNTHENATE TARTRATE therapy ... for, in the early phase of coryza, this simple treatment brings gratifying, often dramatic relief.

In 65% of cases complete remission of symptoms occurs within fifteen minutes after injection of 1 cc of SYNTHENATE TARTRATE-Breon, when administered within twenty-four hours of the first sign of a cold!

Injection is simple...relatively nontoxic...prolonged in effect. SYNTHENATE TARTRATE-Breon increases cardiac efficiency and frequently slows the pulse rate; thus it is effective without appreciably increasing the work of the heart. It does not cause cardiac arrhythmias, does not stimulate the central nervous system, does not produce signs of anxiety.

DOSAGE: 1 cc injected intramuscularly or subcutaneously . . . repeated in 3 or 4 hours, if required.

SYNTHENATE

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TARTRATE SOLUTION

Available at all drug stores, 1 cc ampuls — boxes of 12 and 25.

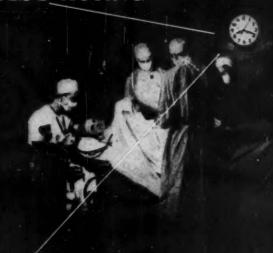
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FAST ACTING



added safety for the patient greater control for the surgeon



In its tast acting control of hemorrhage, KOAGAMIN affords a clearer field for surgery. It reduces bleeding in minutes, regardless of the cause, while Vitamin K, slower in action, is indicated only where prolonged prothrombin time is a factor. When used in conjunction with Vitamin K in such cases, KOAGAMIN effects more rapid control

PREOPERATIVELY minimizes oozing
POSTOPERATIVELY controls secondary bleeding
THERAPEUTICALLY aids control of internal bleeding

An aqueous solution of exalic and malonic acids for parenteral use KOAGAMIN works last at a limb when speeds safety and control are needed

> Supplied in 10 cc. diaphragm-stoppered vials. Comprehensive dosage chart and literature on request



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Available through your Physician's Supply House or your Pharmacist



Greater effectiveness

Oral therapy with Aluminum Penicillin has proved to be effective in fulminating infections such as pneumonial and in other infections due to streptococci, staphylococci and gonococci.2 It rarely causes gastric disturbance or allergic reactions. The patient's bodily and mental comfort is improved because the necessity for frequent injections is eliminated.

The unique advantages of Aluminum Penicillin are that it is not soluble in solutions of acidity corresponding to that of gastric secretion, but is gradually converted into a readily absorbed form in the intestinal tract. These factors provide for maximum utilization of the dosage administered, higher and more prolonged blood levels.3

Sodium benzoate is added because it inhibits the destructive action of intestinal enzymes.4

Each tablet contains: Aluminum Penicillin, 50,000 units; sodium benzoate, 0.3 gram. Supplied in vials of 12 tablets.

Terry, L. L. and Friedman, M. The Military Surgeon, Vol. 103, No. 5, November,

Friedman, M. and Terry, L. L. Southern Medical Journal, Vol. 42, No. 6, June,

Bohls, S. W. and Cook, E. B. M. Texas State Journal of Medicine, Vol. 41, Novem-

ber, 1945, p. 342. Reid, R. D., Felton, L. C. and Pitroff, M. A. Pro. Soc. for Exp. Biol. and Med., Vol. 63, 1946, p. 438.

* Patent applied for.





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long- lasting relief
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SEDO-SPASMOLYTIC

tension and migraine headaches spastic dysmenorrhea, spasms of gastro-intestinal, biliary and genito-urinary tracts, with accompanying nervousness.

By Valoctin tablets 5 grains, each containing 1 gr. Octin mucate and 4 grs. Bromural. DOSE: 1 or 2 tablets at onset of distress. Another tablet after 4 hours if necessary.



VALOCTIN & F. Bihuber, Inc.

BILHUBER-KNOLL CORP. ORANGE, NEW JERSEY

LETTERS TO THE EDITOR

-Continued from page 16a

"This article was read with great interest and profit by us and we are sure it will be considered valuable to the readers of your periodical whom you have done a considerable service by calling to their attention this important but neglected disease.

"You may be interested in knowing the National Multiple Sclerosis Society has been organized with the specific purpose of advancing research and knowledge in general about multiple sclerosis. In addition to publications for patients, a number of monographs are being planned for physicians dealing with rehabilitation and other problems important to patients with multiple sclerosis, and their physicians. The medical material is sent only to physicians, who can secure it by communicating with the Society.

"Patients who join the Society receive a publication, AARMS Forward, which deals with many of the problems and explains to them the research that is going forward in this disease.

"It has been our experience that membership in the organization for the patients with multiple sclerosis has a very salutary psychological effect, as it encourages a note of optimism too long missing in this problem."

> Harold Raoul Wainerdi, M. D. Associate Medical Director (National Multiple Sclerosis Society)

PLAUDIT

"Let me take this opportunity to congratulate you on your excellent journal very informative and useful. I always read it carefully."

Roger A. Schmidt, M. D. San Francisco, Calif.

Q.S.

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FOR LARGE DOSAGE



THE FIRST CLINICALLY PROVEN ENTERIC-COATED ASPIRIN

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ASTERIC Brewer

(5 gr. enteric-coated Aspirin) Allows Greater Dosages— 40, 50, 60, 70 or more grains daily as required where gastric distress and other irritating symptoms resulting from high dosages of plain aspirin tablets are contraindicated.

ASTERIC Brewer

is indicated in the treatment of certain rheumatic disorders requiring maximal dosage of aspirin over long periods. "Enteric-coated aspirin (ASTERIC) has an analgesic effect equal to that of regular aspirin and the onset of its action is only slightly delayed." Clinically it was shown that equal blood levels were obtained."

ASTERIC Brewer

(5 gr. enteric-coated Aspirin) will be found beneficial for those patients suffering from hemorrhagic gastritis resulting from the irritating effects of plain aspirin and for cases of peptic ulcer which require acetylsalicylic acid therapy.

ASTERIC Stewers

(5 gr. enteric-coated marbleized tablets) supplied in bottles of 100 and 1000.

Sample and Literature on request

*Talkov, R. H., Ropes, M. W., and Bauer, W.: The Value of Enteric Coated Aspirin. N.E.J. Med. 242,19 (Jan. 5) 1950.



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BALANCE



The overall virtue of Koromex Jelly and Cream is best emphasized by the evenly tested elements . . . carefully adjusted surface tension, ideal viscosity and highest spermicidal power possible, after dilution . . . which all combine to assure the health and happiness of the patient.

ACTIVE INGREDIENTS: BORIC ACID 2.0% OXYQUINOLIN BENZOATE 0.02% AND PHENYLMERCURIC ACETATE 0.02% IN SUITABLE JELLY OR CREAM BASES



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ATTACK ON

ARTERIOSCLEROSIS

B-TROPIC

potent new therapeutic weapon corrects abnormal fat and oxygen metabolism

By balancing the critical equation between blood cholesterol and phospholipids and stimulating normal cellular oxidation, B-TROPIC corrects the recently clarified metabolic causes of atherosclerosis... the most common form of arteriosclerosis.

B-TROPIC

Two Agreeable Dosage Forms

1. LIPOTROPIC FACTORS

promote normal fat utilization, reduce excessive cholesterol levels, favor phospholipid formation

2. OXYTROPIC FACTORS

regulate intracellular oxidation, synergize lipotropic mechanism, enhance tissue vitality

Capsules

Each capsule contains:

Choline Dihydrogen		90
Citrate	 0.375	Gm.
Inositol	 0.125	Gm.

Thiamine	HC1	1 mg.
Riboflavin		0.5 mg.
Niacin	**********	5 mg.

B-TROPIC AVAILABLE

solution—Bottles containing 1 pt. and 1 gal.

CAPSULES—Bottles of 100, 500, and 1,000.

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Citrate (47% Choline).... 6 Gm.

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Nicotinic Acid...... 20 mg.

Each fluidounce contains:

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LITERATURE ON ATHEROSCLEBORE

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Benzestrol Covers Your Estrogenic Problems



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The Effective, Non-toxic, Synthetic Estrogen

Available in all Dosage Forms:

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Vaginal Tablets: 0.5 mg.

Injectable Solution: 5.0 mg. per cc.

Elixir: 2.0 mg. per teaspoonful.

Average Dose: 1 to 2 mg. or equivalent daily.

*Hufford, A.R.: J.A.M.A., 123, 259, (1943)





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2, 4 · di (p · hydroxyphenyl) · 3 · ethyl hexane Clinical abstracts, literature and samples on request.



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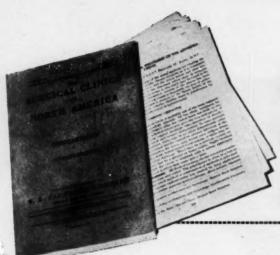
Obocell
a combined hunger
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To depress or curb the appetite by therapeutic means is simply not enough . . . it leaves bulk hunger unsatisfied and the patient continues to overeat.

OBOCELL, based upon the newer concepts of hunger and appetite, supplies methylcellulose (150 mg.), an indigestible, non-nutritive bulking agent, plus dextro-amphetamine phosphate (5 mg.), the most potent agent to curb the appetite. OBOCELL safely guides the obese patient through the psychologic hardship of a reducing regimen by (1) suppressing bulk hunger; (2) by curbing the appetite; (3) with predictable weight loss. Supplied in bottles of 100, 500, 1000 at prescription pharmacies everywhere.

LITERATURE AND SAMPLES ON REQUEST

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dainty, convenient single-dose disposable applicators

westhiazole



by Stein, I. F. and Kaye, B. M.: Su. Clin. North Am. 30:259, 1950.

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WESTHIAZOLE VAGINAL:
a sterile jelly,
10% SULFATHIAZOLE,
4% UREA, 3% LACTIC ACID,
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polyethylene glycol base.

Acidifies, normalizes
vaginal pH, encourages growth
of friendly Doderlein
bacilli, combats secondary
as well as primary infection,
speeds healing.

Pediatric patients geriatric patients and patients who experience difficulty in taking the customary forms of oral antibiotic medication

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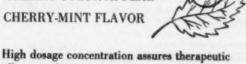
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the only broad-spectrum antibiotic available as an elixir.

One teaspoonful (5 cc.) provides

250 mg. TERRAMYCIN HYDROCHLORIDE

CHERRY-COLOR APPEAL CHERRY-MINT FLAVOR



efficacy without requiring unwieldy dosage schedules. Provides convenience and flexibility in dosage.

Available at prescription pharmacies in bottles containing 1 fl. oz.

Antibiotic Division



CHAS. PFIZER & CO., INC. Brooklyn 6, N.Y.

Anemia the one most common sign







"It is probable that anemia is the one sign most commonly encountered by physicians in patients of any age ..."



Of all the anemias, however, the hypochromic or secondary anemias are encountered most often. Some estimates place their incidence as high as 95%.² In practically any acute or chronic disease, debilitating disorder, and "run down" or lowered resistance state, the secondary or hypochromic anemias must always be held in mind as a possible secondary complication.

Whenever an effective, reliable, and well-tolerated hematinic is required for the prophylaxis or therapy of the secondary or hypochromic anemias, HEMOSULES* 'Warner' are indicated.

The recommended daily dose of 6 HEMOSULES* provides . . .

Ferrous sulfate (15 gr.)	972.0	mg
Liver fraction 2 (15 gr.)	972.0	mg
Folic acid**	1.2	mg
Thiamine hydrochloride (vitamin B.)	6.0	mg
Riboflavin (vitamin B ₂)	6.0	mg
Niacinamidet	24.0	mg
Pyridoxine hydrochloride (vitamin B _a)†	3.0	mg
d-Panthenol (equiv. to 3.0 mg. pantothenic acid) **	2.82	mg
Ascorbic acid (vitamin C)	90.0	mg

^{**}The need for puntothenic acid and folic acid in human nutrition has not been established.

Indications

HEMOSULES* 'Warner' are indicated in anemias secondary to acute or chronic infection, malignancy, acute or chronic blood loss, parasitic infection, malaria, pregnancy, hypothyroidism, inadequate iron intake, and gastrointestinal disease; and chlorosis or idiopathic hypochromic anemia.

Package Information

HEMOSULES* 'Warner,' hematinic capsules, are available in bottles of 96, 250, and 1,000.

References

- Doan, C.A. and Wright, C.S., The Anemic States: Their Causes and Treatment, Med. Clin. N. Amer., (March) 1949, p. 541.
- Kracke, R.R., Diseases of the Blood and Atlas of Hematology, J. P. Lippincott Co., Phila., 2nd ed., 1941, p. 202.

William R. Warner

DIVISION OF WARNER-HUDNUT, INC.

NEW YORK

LOS ANGELES

ST. LOUIS

[†]The minimum daily requirement for nincinamide and pyridoxine hydrochloride has not been established.

^{*}Trade Mark

NEW-Chlorophyll therapy for peptic ulcers!

CHLORESIUM POWDER

EFFECTIVE-

in a recently reported clinical series*, complete healing was obtained in 58 out of 79 cases of long-standing peptic ulcers within 2 to 7 weeks—with new chlorophyll powder!

No special diets were required. No restrictions on smoking, alcoholic beverages or daily activity. Three out of four cases got complete symptomatic relief within one to three days!

Incorporating the same water-soluble chlorophyll derivatives well known to the medical profession in Chloresium Ointment and Chloresium Solution (Plain), Chloresium Powder is a completely nontoxic combination product specifically designed to allow prolonged contact of tissuestimulating chlorophyll with the ulcer crater. At the same time, it provides the essential buffering and protective action found in the usual ulcer medication.

The "Bonus" Action of Chloresium Powder

- Prolonged protective coating (dehydrated powdered okra).
- 2. Prompt antacid action (alum, hydroxide, mag-

nesium trisilicate)—no alkalosis, no acid rebound, no interference with bowel regularity.

PLU5

3. Promotion of granulation tissue (with tissuestimulating chlorophyll). Only Chloresium Powder gives this tissue-stimulating "bonus!"

Chloresium Powder, in this clinical trial, demonstrated its effectiveness to the peptic ulcer patient quickly in the form of complete symptomatic relief. It demonstrated its effectiveness to the physician, under roentgenological examination, in prompt healing of the ulcer crater—usually in 2 to 7 weeks—even in cases which had been resistant to other therapy. (The minimum known history of the ulcers treated was two years.)

The freedom from dietary and other restrictions which Chloresium Powder allows has obvious patient appeal and can greatly simplify the task of insuring patient cooperation.

We invite you to try Chloresium Powder on your most resistant case. Just mail the coupon below for a five-day trial supply.



Ethically promoted. Available at your druggist in slip-label cartons of 25 envelopes (25 doses).

Chloresium Powder

Natural nontoxic chlorophyll therapy for the treatment of peptic ulcers

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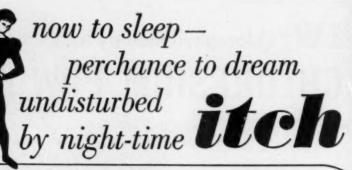
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Please send full-size sample of Chloresium Powder and reprint of the clinician's paper on chlorophyll therapy for peptic ulcers.

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ANTIPRURITIC CREAM

EURAX antipruritic cream, applied to the itching area before retiring, is your patient's best assurance of a full night of undisturbed sleep.

A totally new antipruritic . . . EURAX, original product of Geigy research . . . sets new standards in the treatment of pruritus. In a carefully controlled study¹ EURAX provided "excellent (complete) relief" in 66.2 per cent of cases, and "moderate (considerable) relief" in 27.4 per cent. In most instances a single application ensured relief for 6-8 hours or more. In no case did the cream lose its effectiveness on continued application.

Not an antihistaminic . . . not a -caine derivative . . . not a phenol preparation . . . EURAX gives quicker, longer-lasting itch control with notable absence of local irritation, sensitization or systemic toxicity.³

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- Couperus, M.: J. Invest. Dermat. 13:35, 1949.
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FORMULA: Each enteric-coated tablet or each teaspoonful of chocolate-flavored liquid contains 0.3 Gm. (5 gr.) sodium salicylate U.S.P., and 0.3 Gm. (5 gr.) para-aminobenzoic acid (as the sodium salt).

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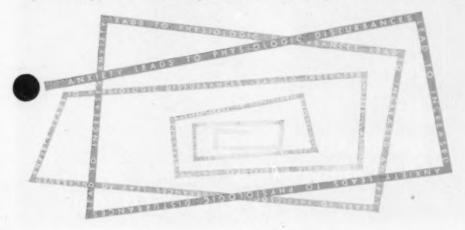
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The studies by Gofman and his co-workers seem to resolve these conflicting reports into an understandable pattern. These studies also give basis for hope for success in the prevention of atherosclerosis.

A short abstract of the paper by Gofman, a booklet on the use of lipotropic agents and a table of high-cholesterol foods and their low-cholesterol substitutes are available. The latter is on a blotter, handy for desk Gofman, J. W. and Associates Science 111:116 (1950)

reference. Since the lay press (Saturday Evening Post, American Weekly and others) have discussed Gofman's paper at length, this concise material may prove helpful in correcting any misconceptions your patients may have gained from their reading.

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An ampul of Protamide was administered intramuscularly daily to thirty-one cases of herpes zoster.

Of the thirty-one cases—twenty-six were relieved of pain in twenty-four hours to four days. Four cases required longer treatment for complete relief. In only one case was pain relief incomplete. (This case may have presented post-herpetic neuralgia, as pain was present for five weeks before treatment. More prolonged therapy is indicated in such cases.)

"The relief of pain was superior to that obtained when using either pituitrin, thiamine chloride, autohemotherapy, sodium iodide or high voltage roentgen therapy. Further, vesicles

HERPES ZOSTER

and crusts disappear much more rapidly than in untreated cases.

"The advantages of Protamide are the simplicity and absence of pain in administration, lack of reactions, and its apparent safety."

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1U.S. Armed Forces Med. Journal, September, 1950

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*MDR - Minimum Doily Requirement †RDA - Recommended Daily Dietary



The Clinical Use of Nitrogen Mustard

THEO. Z. POLLEY, M.D. A. M. BRIXEY, JR., M.D. Soliet, Illinois

Nitrogen Mustard (Beta Chloroethylamine) has slowly but steadily since 1927 (1) gained prominence in the treatment of certain of the miscellaneous malignancies. The therapeutic effectiveness lies not in a complete cure but as a measure of temporary control and palliation in such conditions as Hodgkin's disease, Lymphosarcoma, Chronic Laukemias, Polycythemia Vera, Transitional Cell Carcinomas and certain undifferentiated carcinomas of the testis and lung. During the past year treatment of the abovementioned conditions has advanced rapidly as indicated by the large number of available published reports. It can be generally concluded at present that the drug may be safely administered intravenously, the usual dose being 0.1 mgm. per kilo of body weight, to be given daily for four to six days, and when carefully administered few minor systemic reactions may be anticipated. Favorable comments are found in all the literature as regards good responses against local and systemic manifestations of Hodgkin's disease, Lymphosarcoma and Chronic Lymphatic Leukemia. Certainly the most favorable results may be anticipated in the treatment of Hodgkin's granuloma, especially in those cases which are or have become insensitive to x-ray, and in some cases this insensitivity is abolished following a course of Nitrogen Mustard. The efficacy of the therapy in chronic leukemias has been somewhat promising, yet not spectacular. In the acute leukemias favorable response to this chemical has not been seen.

It might be well at this point to review for a moment the pharmacological activities of the Nitrogen Mustards, which have been summarized by Gilman and Philips (2).

The mode of action, though not clearly understood, is felt to be that of a potent cytotoxic effect on active proliferating cells and cells with mitotic activity. There have been certain changes in cellular metabolism which have been demonstrated and which are a reduction in oxygen consumption, depression of aerobic and anaerobic glycolosis, with inactivation of enzyme systems and inhibitions of mitotic activity. Small doses of HN2 have been known to produce chromosome mutations of the *Drosophila melanogaster*, which are similar to those produced by ultraviolet or x-ray irradiation. Bone marrow de-

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pression with depletion of hematopoietic cells, desquamation and atrophy of the gastro-intestinal mucosa, and testicular involution are the side effects of Nitrogen Mustard therapy. One might note that these changes involve tissues of great cellular activity exceeded perhaps only by the diseased tissue itself and therefore these complications serve to emphasize the action of Nitrogen Mustard on actively proliferating cells.

The dosage schedule of this preparabetachloroethylamine tion. Methyl-bis hydrochloride, which will be referred to as HN2, has been established by the National Research Council as being 0.1 mgm. per kilo of body weight per day for three to four successive days, given intravenously. In a recent paper published by Alpert, Greenspan and Peterson (31), it was reported that they used up to 0.36 mgm. per kilo but that the total dose for one course of treatment did not exceed 46 mgm. with the exception of one patient who received 60 mgm. The technique used by these authors was the standard technique being followed by previous workers in the field. We quote their schedule, for it summarizes the technique used to its best advantage.

"The material in each ampoule was dissolved in 10 cc. of normal saline, producing a concentration of 1 mg. per cc., and the calculated dose was withdrawn into a 10 cc. syringe. The needle was then replaced by another dry one, of No. 22 gauge, in order to avoid introduction of the material into the skin and subcutaneous tissues. The injection was made into the largest available antecubital vein and, after it was completed, blood was drawn back and forth into the syringe in an attempt to dilute further any HN2 remaining in the needle or at the injection site. With this technic, the incidence of thrombophlebitis and subcutaneous reaction was kept at a minimum. In some patients an intravenous infusion of normal saline was started, and the HN2 solution

was injected into the lumen of the rubber tubing or through the air vent. This method gave greater assurance that there was no leakage around the needle, and there were fewer local reactions. The development of nausea and vomiting, which usually occurred between one and three hours after injection, was unpredictable in occurrence and variable in intensity from one patient to another, and often in the same patient during different courses of treatment. Subcutaneous or intramuscular injection of sodium amytal (3.75 to 7.5 grains) was found to be the most effective means of reducing nausea. The administration of atropine or large doses of pyridoxine occasionally afforded the patients some relief. Benadryl was ineffective in combating the gastro-intestinal symptoms" (31).

In view of the many experimental uses of HN2, only those diseases will be discussed in which HN2 is a relatively useful agent. This list includes Hodgkin's Disease, Lymphosarcoma, Mycosis Fungoides, Polycythemia Vera, Chronic Lymphatic and Myelogenous Leukemia, and Bronchiogenic Carcinoma.

Hodgkin's Disease (17)(18)(19) early and localized Hodgkin's disease xray therapy is the treatment of choice. In cases of generalized disease with enlarged nodes, liver and spleen with systemic manifestations such as fever, weakness, anorexia, and weight loss, an adequate course of therapy with HN2 will produce some clinical improvement in eighty to ninety per cent of the cases. The usual period of expected improvement is from three to eight weeks though remissions of one or more years have been produced. It is immediately following therapy and during the remissions that almost miraculous results are observed in the cases which respond from the standpoint of rapid alleviation of systemic symptoms, with tumor regression and allied objective improvement.

During such a period of remission we

ourselves have noted not only complete disappearance of all palpable nodes and all systemic complaints but complete clearing of a chylothorax produced by mediastinal node enlargement with subsequent pressure and obstruction of the thoracic duct with a spilling over of the chyle into the left pleural cavity. This condition in a twenty-year-old student nurse of ours has not recurred. It was interesting to note, too, that bony destruction caused by infiltrating Hodgkin's disease revealed x-ray signs of re-ossification with subsidence of the signs and symptoms of posterior nerve root involvement.

Another specific case with interesting clinical ramifications was a patient treated by one of us (32). This patient had a marked Lymphoblastoma Cutis involving the skin of the entire body. The condition receded with the use of Nitrogen Mustard therapy. Although the results were promising after the first course of therapy, which was in April, 1948, a second course three months later resulted in complete remission lasting more than seven months following the last injection. During this time the patient's skin had remained soft and pliable, and microscopic examination of the skin and lymph nodes showed an almost complete restitution of normal structure. One interesting complication which occured in this particular case was a testicular atrophy. This has been noted in up to ninety per cent of the cases treated with Nitrogen Mustard, whereas this has been observed in no more than 57 per cent treated in the usual manner.

In the management of Hodgkin's disease one must not lose sight of the fact that HN2 may be used as an adjunct to x-ray therapy. All patients with advanced Hodgkin's disease deserve an adequate trial of HN2 when radiotherapy no longer proves useful. If a significant period of improvement results, it is likely that the patient will respond to

further courses of HN2 or x-ray therapy. This may be of some prognostic value. The longer the remission following the use of HN2, the greater the possibility of producing further remissions. X-ray therapy will rarely prove beneficial in cases in which the patient fails to show any response to an adequate course of HN2. Though HN2 does not materially alter the course of Hodgkin's disease we must admit that it has certainly proved itself in some cases by the fact that it relieves suffering as produced by nerve root involvement, and the severe allied systemic reactions which the disease produces. Affording comfort to the patient, in our mind, justifies its use in spite of its toxic manifestations. It has been reported recently that the life span of Hodgkin's cases has been shortened by the use of HN2 since the most favorable time for radiation therapy is consumed by courses of HN2 therapy.

Lymphosarcoma Under this heading will be included a host of allied diseases including Leukolymphosarcoma, Reticulum Cell Sarcoma, Lymphocytic Lymphosarcoma, and Giant Follicular Lymphoma. In this group, as we all know, the disease may run a widely different clinical course some are rapidly lethal while others may be present for many years in a relatively benign state. These conditions are all best treated by localized irradiation. It has been found according to the investigators in this field that if a case responds poorly to x-ray, either because the condition is highly aggressive or rapidly disseminating, HN2 proves of little avail in therapy. The rapidly growing tumors may shrink remarkably following a course of therapy but recur within a few days (20) (21) (22) (23).

In the slowly progressing Lymphosarcoma HN2 has produced a partial regression of the disease with systemic improvement for periods of six to eighteen months according to Karnofsky et al. (22). It was found that HN2 may be effective in only twenty per cent of the terminal cases or in the cases which apparently do not respond to x-ray treatment. In these cases caution should be exercised regarding the occasional unpredictable toxic responses. Certainly the responses in Hodgkin's disease have been more striking than those occurring in the therapy of Lymphosarcoma.

Tumors, as cited previously in the case of the student nurse, which produce symptoms due to local pressure, may be rapidly affected by HN2 without producing that period of edema preceding the tumor regression which follows in the case of radio-sensitive tumors.

HN2 has been used as an emergency measure in tracheal pressure due to Lymphosarcoma, and in such cases it may rapidly relieve obstruction and permit the safer continuation of localized x-ray therapy (23).

Mycosis Fungoides This condition is of an uncertain nature and it has been known to exist for a number of years as a very slowly progressive skin process, then suddenly exacerbate and terminate as a Reticulum Cell Sarcoma. It is well known that for localized skin manifestations x-ray therapy has proved useful. In patients with extensive skin involvement, improvement for one to five months, with shrinkage of the skin lesions and relief of pruritus, has been produced with HN2 in perhaps half the cases (33) (34) (35). In general, patients with extensive skin lesions diagnosed as Mycosis Fungoides, and no longer suitable for x-ray therapy, merit a trial with HN2.

Polycythemia Vera This disease, though there are many methods of management and though P32 is currently regarded by many as the therapy of choice, lends itself to HN2 therapy, which will produce remissions lasting from three to five months. P32 will produce remissions lasting from six to twelve months in duration and can be given without discomfort to the patient.

Bronchiogenic Carcinoma In far

advanced Bronchiogenic (24) (25) (26) Carcinoma of the lung HN2 has begun to gain favor in cases where palliation forms the main recourse to therapy. Karnofsky et al. (24) report that about sixty to sixtyfive per cent of the patients have experienced symptomatic relief in the reduction of cough, pain, and dyspnea with an increase in strength and appetite. Included were eleven cases with symptoms of superior vena caval obstruction, eight of which were improved following therapy. The improvements noted in these groups treated were a decrease in pulmonary densities and increased aeration of the lungs, decrease in pleural effusion, regression of metastases, reduction of elevated venous pressure due to superior caval obstruction and in one case a remission of neurological signs due to a cerebral metastasis. The remission lasted from two to twelve weeks with an average of about five weeks. Subsequent courses of treatment have proven less successful and even in the most favorable cases life was prolonged for only a few months. HN2 has proved of some help in the management of anaplastic or oat-cell bronchiogenic carcinoma, which is usually unsuitable for x-ray therapy.

Chronic Lymphatic Leukemia (26)(27)(28) In this disease radical medical therapy should always be tempered and administered conservatively. The effective agents used are x-rays, P32, Urethane. and HN2. Frequently a relatively small amount of therapy may produce partial but quite satisfactory clinical improvement, whereas larger doses may often severely affect normal hematopoietic function, precipitating anemia, thrombocytopenia and hemorrhage. X-ray and radioactive phosphorus have been the most generally effective types of therapy. HN2 and Urethane have not been as consistently useful, yet they have produced prolonged clinical improvement with regression of enlarged organs, fall in white blood count, and a rise in hemoglobin level.

Chronic Myelogenous Leukemia

The early or responsive stage of chronic Myelogenous Leukemia may be treated with P32, x-rays, Urethane or HN2. The response will reduce the size of the spleen, produce a fall in the white blood count, a rise in the hemoglobin level and a general increase in strength. Irradiation of the spleen aside from being the simplest form of therapy is without doubt the most practical. P32 is equally effective at times and does not produce the side reactions of nausea and vomiting (18). Urethane, an inexpensive preparation, can be administered orally and on an outpatient basis and after three to four weeks of a daily dosage of three to six grams remissions may appear and improvement can continue for long periods on maintenance therapy. HN2 can be administered following this period of Urethane therapy, and although nausea and vomiting often occur during the few days of therapy the course can be rapidly completed. The remissions last from one to four months, a somewhat shorter period than we expect following adequate x-ray therapy (29). It has been suggested that the most satisfactory remissions from the use of HN2 have been obtained by gradually bringing the total white count down to a range of 5,000 to 10,000 and holding it there for a period of several weeks by maintenance HN2 therapy. It has been found possible to give small doses of HN2 at two to six week intervals as maintenance therapy (30).

As the disease approaches its terminal stage with lymphadenopathy, anemia, hemorrhages and an enlarged spleen with an increase in immature cells in the bone marrow and peripheral blood, the available therapeutic agents become less and less effective. During this terminal stage HN2 may, by permitting a rapid and wellcontrolled course of therapy, be useful in determining whether the disease can. with vigorous treatment, show any further response.

Conclusion Nitrogen Mustards are highly toxic substances and the therapeutic dosage is based upon a narrow margin of safety. Adequate precautions must be taken to prevent the solutions from coming in contact with the patient's skin, or from escaping into the tissues about the vein. Even with these precautions some workers have reported severe local complications and venous thromboses. The systemic reactions though not serious or dangerous are at least as severe as irradiation sickness. Blood counts must be checked frequently since there is a real danger of producing a fatal leukopenia or a severe thrombopenia, and possibly an aplastic anemia. The fact that the full manifestation of bone marrow suppression may not be evident for almost a month after a course of Nitrogen Mustard indicates that one cannot be too cautious and must use good judgment in advising retreatment (3).

Summary A review of the literature on the use of Nitrogen Mustard in temporarily controlling and in producing palliation of extensive and inoperable neoplastic disease has been described and discussed. The indications for the use of Nitrogen Mustard in the management of Hodgkin's Disease, Carcinoma, phosarcoma, Leukemia, Lymphoma and related diseases and the results which one might expect from its administration are reviewed.

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Call for Cooperation in Occupational Cancer Control

With the knowledge that about 200 chemicals are possible cancer producing substances, the director of the National Cancer Institute, Bethesda, Md., recently called for the joint efforts of industrial and labor organizations combined with local, private and state health agencies to aid in the further discovery and control of these agents.

Research needed to solve the problem of environmental and occupational cancer presents a challenge of "tremendous proportions", says Dr John R. Heller, Jr., in Archives of Industrial Hygiene and Occupational Medicine, published by the American Medical Association.

More research into the background and case histories of cancer patients, laboratory testing of suspected cancer-producing agents, follow-up studies of exposed workers and studies of safety procedures and preventive measures in plants where such substances are handled are necessary, believes Dr. Heller, to "solve the mystery" of environmental and occupational cancer.

Therapy and Diagnosis

A Review of New Developments in 1950

This summarization attempts to review the essential information on new developments during the past year and is designed as a time-saving refresher for the busy practitioner.

This review of new developments in drugs and technics used in therapy outlines briefly the progress which has been made during the past year. No attempt has been made to include the myriad of new products made available. Selection of the items included was made on the basis of a new theory or a new entity entirely. Many of the compounds described are still undergoing animal experimentation or preliminary clinical trials. It is possible that they may never advance beyond this stage but they are included because they are indicative of possible present and future trends.

Whenever possible the new advances will be considered under the group signifying their major action or use. Since there are so many classifications to be considered they will be taken alphabetically.

ADRENERGIC BLOCKING DRUGS

SY-2 A new adrenergic blocking drug, N-ethyl-N-(2-chloroethyl)-benzhydrylamine hydrochloride, similar to Dibenamine in potency, duration of action and specificity

is under investigation. It is practically devoid of antihistamine and antiacetylcholine properties. Animal experiments have shown that this drug has a low oral acute toxicity in mice. Comparatively small doses reduced the toxicity of epinephrine in mice and moderate doses failed diminish histamine-induced chiospasm in guinea pigs. In intravenous doses of 5.0 to 20.0 mg./Kg. the drug induced epinephrine reversal, prevented pressor responses to anoxia and definitely reduced pressor responses to splanchnic stimulation in dogs. In cats, doses of 20.0 mg./Kg. intravenously induced epinephrine reversal and diminished or blocked responses of the nictitating membrane to injections of epinephrine and stimulation of the cervical sympathetic nerves.1

ALCOHOLISM

Hormones For some time the alcoholic has been considered to be a psychiatric problem. However, a recent study of two thousand acute and chronic alcoholics by Smith of New York University-Bellevue Medical Center has revealed either improper stimulation or deficiency of the adrenals and sex glands. In alcoholism the pituitary does not produce

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sufficient hormone to stimulate the adrenals and sex glands, resulting in uneasiness and tension. This, in turn, leads to drink. Administration of ACTH and cortisone, sex hormones and ACE (adrenal cortical extract) and vitamin C have brought about response in twenty-four hours.

ANALGESICS

Nisentil A new obstetrical analgesic, 1, 3-dimethyl-4-phenyl-4-propionoxy-piperidine hydrochloride (dl-alpha form) has recently been made available. Its action resembles that of morphine. For optimum results it should be given subcutaneously in doses of 30 mg. When given both orally and subcutaneously a lesser percentage of good results was obtained. When compared with morphine, methadone and combinations of morphine with neostigmine or scopolamine it appeared to produce a greater percentage of good results.²

Subdamine Another new analgesic and sedative is being investigated particularly for its properties in relieving the symptoms of anxiety and tension in psychoneurotic patients. It is of value as well in certain organic diseases such as hypertension and the climacteric. Chemically this new drug is 1-diethylcarbamylpiperazine. It possesses potent sedative activity but low somnifacient activity. Its toxicity also is low.

Sixty-three of 83 patients (76 per cent) treated with this drug reported improvement to some degree. Eighty-six per cent of 66 patients with functional manifestations predominating showed some relief of symptoms. Small doses of phenobarbital achieved about the same results but in some cases it produced drowsiness which does not occur with the new drug. The only side reactions observed were mild disorientation at night, nausea, dizziness and vomiting. The first mentioned was the only severe reaction, the others occuring in only a few patients.³

ANESTHETICS

Procaine Derivatives The two most active local anesthetics in use at present are tetracaine and dibucaine. Certain of the ortho-substituted para-aminobenzoates and some of their analogs (procaine derivatives) appear to be even more potent. They have been synthesized and tested for their activity as local anesthetics. A substantial increase in activity was produced by substituting an ortho-hydroxy group in procaine. The ortho-hexyloxy compound is approximately 100 times as active as procaine. Tests for toxicity have shown that it is proportional to the activity and based on the activity these compounds are less toxic than procaine. The only exception is the ortho-methoxy compound. The ortho-alkoxy derivatives of procaine apparently are less irritating locally since this effect does not seem to have any direct dependence upon activity or toxicity. A good activity irritation ratio is exhibited by the most active compounds. The ortho-propoxy analog has an activity of about 10 times that of procaine but it is only twice as irritating.4

Surital Sodium In all fields of medicine the search goes on for the ideal drug for some specific use. Just so in the field of anesthesia, it is thought that the barbituric acid derivatives now employed parenterally do not entirely meet the specifications of the ideal agent. Consequently, a new drug, sodium 5-allyl-5-(1-methylbutyl)-2-thiobarbiturate, is being evaluated. The drug was given by intermittent intravenous injection of a concentrated (2-2.5 per cent) solution and by continuous intravenous drip of a dilute solution (0.3 per cent). Smooth, rapid induction occurred when 3 to 10 cc. (60-250 mg.) of the 2.5 per cent solution was given preceding inhalation anesthesia.

The new drug was tested on 1200 patients and was used in the following ways: for the induction of general anesthesia; for induction and endotracheal intubation; with regional anesthesia; for complete maintenance of anesthesia with nitrous oxide-oxygen, with curare; and in anticonvulsant therapy. Encouraging results were observed when it was administered rectally to children.

Although this new drug does not necessarily meet the ideal requirements, it does have certain advantages such as rapid awakening from a comparable plane of anesthesia, more rapid restoration of spontaneous breathing following large doses administered rapidly, less frequent circulatory depression when given in equivalent doses and the more benign character of the laryngospasm.⁵

ANTIBIOTICS

Diplomycin First isolated from a diplococcus in 1945 by Noster ,diplomycin is now being tested in the surgical clinic of AArhus Kommunehospital, Copenhagen in the treatment of 150 patients with different infectious diseases. This new antibiotic appears to possess a pronounced antibacterial action on gram-positive and gram-negative micro-organisms and on tubercle bacilli. In addition, bacterial resistance does not develop and therefore it has been shown to be effective in treating cases in which bacterial resistance to penicillin and streptomycin has developed. It has only slight toxicity. Chronic ulcers of the leg and other localized infections have been treated effectively with diplomycin in ointment form. The clinical effect of intravenous injections of diplomycin filtrates in infections such as abscesses, mastitis and osteomyelitis was often equal to that attained with penicillin. In treating B. coli infections of the urinary tract its effectiveness was equal to that of streptomycin and in some instances even better. In addition, it did not produce the serious side effects which the latter does.

Fungicidin Another new antibiotic agent recently isolated is fungicidin. To date it appears to differ from all other antibiotics. It is effective in vitro against a large number of nonpathogenic and pathogenic fungi, including Candida albicans, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatitidis, Coccidioides immitis, Paracoccidioides brasiliensis, Trichophyton rubrum, (purpureum), and T. mentagrophytes (gypseum). In higher concentrations it has not shown much activity against some of the common bacteria such as Staphylococcus aureas, Salmonella paratyphi, B. S. typhosa, Shigella paradysenteriae, and Bacterium coli. Because of the unusual activity in vitro fungicidin is being investigated for possible therapeutic value.6

Hydroxystreptomycin Hydroxystreptomycin has been isolated from a new species of Streptomyces found in Japanese soil. It has been named hydroxystreptomycin because of its composition and the nature of its degradation products. It resembles streptomycin in composition, optical rotation and biological potency. The trihydrochloride of hydroxystreptomycin, when assayed against Bacillus subtilis, was found to be equivalent to 784 micrograms of streptomycin base per milligram. For streptomycin trihydrochloride the corresponding value is 842 micrograms per milligram. It is hoped that animal experiments and clinical studies will reveal that this compound does not possess the disadvantages of streptomycin.

Lupulon The search for the ideal drug in tuberculosis therapy continues. Another new antibiotic has been shown to have some effect in this disease. Given the name lupulon, it is one of the two antibiotics derived from the soft resins of hops, Humulus lupulus. It is a colorless, odorless and tasteless crystalline substance.

When tested on mice it was found that one-tenth of the acute LD₅₀ could be given intramuscularly every day for 4 weeks without gross evidence of harmful effects. When the tissues of the mice were examined histopathologically small

areas of leukocytic infiltration in the liver and foci of degeneration in the renal tubules were observed.

In vitro and in vivo tests showed promising effects by lupulon on tubercle bacilli. From these observations it was thought that lupulon might have some effect on tuberculosis in humans. Its greater solubility in lipoids might allow for greater penetration of the waxy coat of the mycobacteria.

The 10 patients selected were from both sexes and varied in age from 25 to 43 years. Of the 10, 9 had moderately advanced pulmonary tuberculosis and one had tuberculous laryngitis. One had minimal tracheobronchial disease in addition to the pulmonary disease.

The antibiotic was given in gelatin capsules each containing approximately 0.5 Gm. It was administered orally in 1 Gm. dosages every 4 hours from 6 Å.M. to 10 P. M. so that each patient received 5 Gm. daily regardless of weight. Five patients were given the drug for 3 months, 1 for 2 months, 2 for 50 days and 2 a week or less. Development of complications or side reactions necessitated discontinuing the drug in the last 4 patients.

Blood level tests revealed detectable amounts of the antibiotic in 7 patients tested at regular intervals for a period of 8 weeks. The levels varied from 1.9 to 6.5 gamma per ml. These values were beyond the range of the sera obtained from untreated patients.

All of the patients were examined thoroughly and all of the standard tests were conducted. In 3 patients treated with lupulon there were observed significant decreases in the daily volume of sputum and in the frequency and intensity of the cough. Three patients lost 5½ to 9 pounds whereas the others did not change weight to any significant extent. X-ray examination revealed signs of improvement of the pulmonary lesion in 1 patient. In the others no observed changes could be credited to the medication. No

hepatic or renal function alterations occurred as a result of therapy. Electrocardiograms also revealed no changes.

Three patients developed a negative sputum after therapy but the rest showed little change. No signs of toxicity to the liver, kidney, bone marrow or myocardium were observed.

However, there was a certain amount of gastro-intestinal irritation caused by the antibiotic. There was an epigastric sensation of burning and lower abdominal cramping which developed within 5 minutes to 6 hours after the first dose. Watery diarrhea sometimes accompanied these symptoms and it could not be completely controlled by bismuth subcarbonate or other agents. Some patients experienced nausea and vomiting which continued for 2 days to 11/2 weeks. In 2 patients therapy was stopped because of the severe gastrointestinal disturbance. After the symptoms stopped the patients continued to have a mild loss of appetite. Transient mild frontal headaches were experienced by two patients and lightheadedness by 2 others. Slight somnolence was observed by 2 patients. One patient developed an erythematous macular rash which lasted 2 days and a generalized myalgia for 5 days. Transient eosinophilia was observed in 2 other patients.

Although these investigations are only in the preliminary stages and no definite conclusions can be drawn the results observed are sufficiently encouraging as to lead to further studies. The possibility of drug resistance is now being investigated. However, until more is known about lupulon it should not be used in treating tuberculosis except for investigative purposes.⁷

Nemotinic Acid, Nemotin Nemotinic acid and nemotin are antibiotics which have been isolated from culture liquids of *Poria tenuis*, *Poria corticola*, and an unidentified Basidiomycete from white cedar ("fungus B-841"). They differ markedly in their antifungal action.

However, they have shown effects against Mycobacterium tuberculosis.

Thiolutin Another new antibiotic, reported at a recent meeting of the American Chemical Society, is thiolutin, isolated from strains of Streptomyces albus. It inhibits Gram-positive and Gram-negative bacteria as well as fungi.⁸

Prodigiosin Botts and Lack of the Birmingham Veterans Administration Hospital, Van Nuys, California, have reported that a dye, extracted from bacteria, B. prodigiosus, is effective in vivo and in vitro against the highly infectious San Joaquin or valley fever called coccidioidomycosis. The new antibiotic is named prodigiosin.

Synergism Synergism between drugs is not new, by any means. However, during the past year synergism between various antibiotics and between antibiotics and other drugs has been reported. Penicillin and bacitracin have been shown to be more effective than either antibiotic alone in certain diseases such as subacute bacterial endocarditis. It is believed to be the first between antibiotics to have been reported. It is considered to be a true synergism in that the two can be

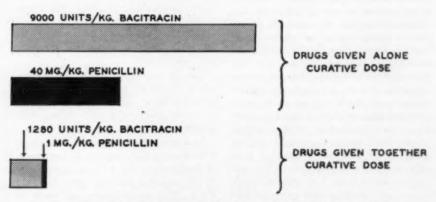
given in smaller quantities than are curative for either drug alone but together they effect a cure.

The synergistic effects of bacitracin and penicillin were demonstrated first on rabbits infected with Treponema pallidum. It was found that the curative dose of bacitracin was about 9000 units/Kg. and that of penicillin was 30-40 mg./Kg. When given together cure was effected with as little as 1 mg./Kg. of penicillin and 1.250 units/Kg. of bacitracin. Thus the synergistic effect of the two antibiotics resulted in a need for only 1/40th as much penicillin and 1/7th as much bacitracin. An increase in the penicillin dosage to 1 to 4 to 16 mg./Kg. reduced the dosage of bacitracin further from 1280 to 840 to 480 units/Kg.

In vitro experiments with 18 strains of alpha and gamma hemolytic streptococci also revealed a synergistic effect. This effect also has been reported in in vitro experiments and clinically in vivo with numerous strains of staphylococci, Cl. welchii and occasionally with hemolytic streptococci.

This phenomenon will undoubtedly prove to be of value in cases where the

CHART SHOWING SYNERGISM OF DRUGS



The synergistic effects of these drugs were first demonstrated in experiments on rabbits infected with Treponema pallidum.

organism is resistant to penicillin but sensitive to bacitracin. Either antibiotic alone in moderate doses in such instances would probably be ineffective in controlling the infection.

Clinical trials are now underway to determine the possible uses of this synergistic effect. Representative cases already reported include a streptococcal infection which did not respond to 300,000 units of penicillin daily. This dosage was increased in 3 days to as high as 1,200,-000 units and continued for 6 days. The temperature still was elevated and the blood culture was positive. Administration of 1,200,000 units of penicillin and 6.000 units of bacitracin (divided into 3 equal doses) daily resulted in negative blood cultures in 10 days. In an infection caused by an enterococcus type of streptococcus which did not respond to penicillin negative blood cultures were achieved in 6 days by supplemental doses of 6,000 units of bacitracin daily.9

Penicillin and dihydrostreptomycin have been combined for their synergistic effect in the treatment of mixed infections due to Gram-positive and Gram-negative organisms, such as subacute bacterial endocarditis, urinary tract infections, and also in the preparation and protection of surgical sites.

In a study of the effects of the two drugs together it was revealed that the combined effect on enterococci is greater than a summation of the effects of the individual drugs. Streptomycin, in the concentrations employed, had no effect and penicillin was in the optimal zone for the organism so that no increase in concentration would be of any value. Thus the increased effect must be a true synergism. The rapid sterilization of the medium (rapid death of the organisms) is indicative of at least potentiation of penicillin action by streptomycin. The next question which arises is whether the viable enterococci remaining after treatment with penicillin alone are resistant mutants and,

consequently, are able to multiply. If this is so, then the streptomycin when mixed with penicillin is simply affecting penicillin-resistant organisms. Experiments long these lines revealed that this is not the case. The streptomycin-penicillin synergism on enterococci increases the bactericidal rate beyond that which can be obtained with penicillin alone. 10

When the therapeutic effect of paraaminosalicylic acid (PAS) given orally was compared with that of streptomycin given subcutaneously the latter was found to be 3 to 6 times more active. When both were given subcutaneously streptomycin was five times more active.

Unfortunately, although streptomycin is more potent, the organisms do develop a resistance to it whereas with PAS this does not occur. Once the resistant organisms develop therapy with streptomycin is ineffective. It is generally agreed that 50 to 70 per cent of the patients who continue to discharge tubercle bacilli after 120 days of therapy will have streptomycin-resistant strains. In a large series of patients studied by the Veterans Administration about 60 per cent of the positive cultures from patients treated for 3 months showed resistance in vitro to 10 or more micrograms of streptomycin per ml. of medium. This resistance to the human type H 37 Rv was retarded when diaminodiphenylsulfone was added to the medium. When streptomycin and sulfathiazole were used the resistance of the avian tubercle bacillus and M. ranae also was retarded.

Thus it appeared obvious that streptomycin should be used along with other antituberculous agents in order to delay or prevent the "development of streptomycin-resistant strains.

In a series of patients with tuberculosis, PAS, Promin and streptomycin were given in combination. The PAS was given orally in the maximal tolerated dose (5 to 10 Gm.). The streptomycin was given in doses of 0.5 Gm. twice daily, intramus-

cularly to some and 0.5 Gm. once daily to others. Promin was given in daily dosage of 5 Gm. intravenously for the first 14 days of a 21 day period. No evidence was observed that any of the drugs increased the toxicity of the others.

By means of cultures the organisms were studied for resistance. At the end of three months of therapy only one patient showed streptomycin-resistant tubercle bacilli and 3 additional patients developed these during the sixth month of therapy. These results appeared promising and led to further studies.

A study of the combined therapy of PAS and streptomycin, in guinea pigs, has shown that the two drugs produce a therapeutic effect better than that produced by either drug alone in the same doses and that the results of this combined therapy are comparable to those obtained with streptomycin alone. Thus it appears possible to give, along with PAS, smaller doses of streptomycin than would be given alone and in this way the hazard of toxic effects is reduced and the development of resistant forms delayed. Dihydrostreptomycin may be used instead of streptomycin. Thus the hazard of toxic effects is further reduced. However, the possibility of resistant forms developing is not diminished.10a

Recently penicillin has been made available in combination with the three sulfonamides: sulfamerazine, sulfadiazine sulfamethazine for simultaneous treatment of infections where oral administration of penicillin and the sulfonamides is indicated. This combination is recommended for treatment of pneumonia, gonorrhea, mastoiditis, scarlet fever and urinary tract infections and as a prophylactic measure before and after tooth extraction, tonsillectomy, cesarean section and minor surgical procedures.11, 12

This synergistic effect of antibiotics for each other, however, cannot be taken for granted. Some, when given together, may be less effective than one alone or even

neutralize each other. In experiments on enterococci with chloramphenicol alone in concentrations of 10 mcg/ml. no significant effect was observed. Although there was a noticeable effect when this concentration of chloramphenical was mixed with 6 mcg./ml. of penicillin, further tests revealed that it was less than with penicillin alone. It required 6 to 12 days with the penicillin-chloramphenicol mixture to achieve the same low number of viable enterococci obtained with penicillin alone in 24 hours. From these experiments it could be assumed that chloramphenicol in some way inhibited the bactericidal effects of penicillin on enterococci. This antagonistic action was observed with varying concentrations of both antibiotics and in varying degrees with all nine strains of enterococci.

Another interesting observation of these studies was that the chloramphenicolpenicillin mixture caused a slow but steady decrease of the bacterial population whereas penicillin alone resulted in a great increase after the sharp decline originally observed. Thus the mixture was equal to high concentrations of penicillin such as 300 mcg./ml. However, the number of viable bacteria decreased more slowly with the mixture and with high concentrations of penicillin than they did at the optimal concentration of penicillin alone (6 mcg./ml.) and all the enterococci were killed after long periods of incubation. Thus it was shown that not all of the antibiotics are synergistic in action but that some may be antagonistic.

Terramycin Streptomyces rimosus, another actinomycete, has been isolated from soil and found to produce a crystalline antibiotic. Because of its derivation it was named terramycin.

Terramycin is a relatively non-toxic antibiotic as shown by extensive animal studies and clinical observations in more than 350 patients. No toxic reactions have been observed when sodium terramycin

or terramycin hydrochloride was orally administered to dogs in dosages of 80 to 500 mg./Kg. of body weight. Some toxic symptoms were observed, however, in a small percentage of animals given 80 to 160 mg./Kg. of body weight of sodium terramycin intramuscularly over long periods of time.

Studies of the absorption and excretion of terramycin in dogs and rabbits have indicated that it is absorbed rapidly throughout the body when given orally or parenterally. It is excreted in a biologically active form.

Studies have indicated (a) that maximum concentrations of terramycin may be detected in the serum of most patients receiving single oral doses of 25 to 50 mg. of terramycin hydrochloride per Kg. of body weight, within 2 hours after administration; (b) that the maximum concentrations achieved after administration of such doses are 5 to 6 and 10 to 20 mcg. per ml. respectively; (c) that after maximum serum concentrations are attained, the levels remain at a plateau for 2 to 4 hours and then decline; (d) that the drug is present in high concentrations in the urine within 2 hours after administration.

Mild gastrointestinal disturbances have been observed in a small percentage of patients. Looseness of the stools was the most common reaction reported. In some cases there was mild nausea and vomiting which in most instances occurred when the drug was taken on an empty stomach. By administering terramycin just prior to a light meal these reactions usually were avoided. When nausea and vomiting did occur they usually were more severe in the first day or two and then disappeared. It has been suggested that the frequency and severity of these reactions may vary directly with the size of the daily dose since no such reactions occurred following dosages of 1 and 2 Gm. daily.

Terramycin is indicated in the therapy of disease caused by many of the Gram-

positive and Gram-negative bacteria, both aerobic and anaerobic; the rickettsiae and certain viruses. At present, the recommended oral dose is 2 to 3 Gm. daily in divided doses given every 6 hours for acute infections. For severe infections double the quantity may be necessary. Adult and children's dosages are the same. Just as with the other antibiotics the dosage in many cases will need to be adjusted for the patient. Therapy should be continued for at least 48 hours after the temperature has returned to the normal level and the acute symptoms have disappeared. All dosages mentioned are in terms of weight of pure terramycin. The intravenous form is indicated particularly in the treatment of peritonitis and in the prophylactic sterilization of the intestines before and after abdominal surgery.

The most recent report on this antibiotic reveals that it is of value in treating eye infections such as trachoma, conjunctivitis caused by the pus-forming staphylococcus, sometimes found with other micro-organisms; deep-seated eye troubles, such as ulcers and similar conditions which may occur in areas difficult to get at; a wide variety of infections and inflammations of the conjunctiva, outer eye surfaces, of the tear sac, and of the minute passages leading to and from the eye; infections following external eye damage, as well as involvements of the eve in venereal disease. In some severe cases terramycin was given orally as well as topically in an eye drop or ophthalmic ointment. For the preparation of the eye drop the antibiotic has been made available in a dry mixture of the crystalline hydrochloride and a sodium borate-sodium chloride buffer. When dissolved in 5 cc. of Water for Injection U.S.P., one cc. provides the equivalent of 5 mg. of pure terramycin. The crystalline hydrochloride also is available suspended in a petrolatum base. Each gram contains the equivalent of 1 mg. of

pure terramycin. Crystalline terramycin hydrochloride is well tolerated by the mucous membranes and other eye tissues.

A topical ointment form is indicated for treating local infections and a troche form for oral, dental and throat infections.¹³

Thrombodent Dental Cones To accelerate firm clot formation and minimize infection following oral surgery there is now available a dental cone containing 1 unit of human thrombin, enough to clot 1 cc., of normal blood in less than one minute, combined with 1 mg. of tyrothricin, which is effective against many of the microorganisms present in the oral cavity that may contaminate postoperative dental wounds. Because they are so highly absorbent they are protected from moisture by a desiccant in a pocket at the bottom of the bottle and the new type polyethylene snap cap, an almost perfect barrier to water vapor and air.14

Viomycin More than 100,000 samples of soil have been processed for antibiotic activity but only 84 molds from this group were found worthy of further investigation. Of the 84 it was found that only two possessed sufficient activity as to warrant clinical trial. These were the groups producing terramycin and viomycin.

Viomycin was isolated from a sample of soil obtained in Cuba. At the present it is difficult to make any prediction as to its possible value in humans since the tests have been so limited. In animals viomycin has been shown to suppress tuberculosis. Mice and guinea pigs were used for these protection tests. Viomycin is believed to be effective against streptomycin-sensitive and streptomycin-resistant strains as shown by both in vitro and animal tests. This is indeed an important property.

Although further clinical studies are necessary to determine its effectiveness in humans the clinical trials thus far have revealed that it can be given to humans for prolonged periods of time.15

ANTICOAGULANT

Heparinoid Experiments are now in progress on a new, synthetic anticoagulant, heparinoid. Chemically it is a polysulfuric ester of polyanhydromannuronic acid obtained as a water-soluble sodium salt.

Eleven patients were selected for the first clinical trials. They were given intravenously a solution of the compound 25 times. The dosage necessary to prolong the clotting time 2 to 3 times was found to be 5-10 mg./Kg. As with most drugs, however, the response varied in some of the patients. Although this dosage is approximately 13 times that of the sodium salt of heparin required for the same effect the results may be more prolonged since they lasted for 4 to 8 hours. Only 3 patients experienced any toxic reaction and 2 were mild.

Phenylindandione Another new anticoagulant being tested is phenylindandione. It appears to have an action which is intermediate between those of heparin and dicumarol. However, it resembles dicumarol more closely. The first dose given is 200 mg. followed by 65 mg. dosages daily for maintenance. In different individuals the rapidity of action was observed to vary. The desired prothrombin level was attained in 10 to 20 hours in 18 patients; in 20 to 28 hours in 20; in 29 to 40 hours in 7; and in 40 to 50 hours in 3.16

Tromexan Bis-3', (oxycoumarinyl) ethyl actate also known as B.O.E.A. has been shown to have anticoagulant properties. Although it appears to more closely approach the ideal it is four times less active than dicumarol. It is necessary also that all the precautions accompanying anticoagulant therapy be employed. B.O.E.A. is more rapidly eliminated than is dicumarol so that any hemorrhaging should be less severe.

B.O.E.A. has been tested on patients with venous thrombosis, pulmonary em-

boli, arterial thrombosis or emboli. The treatment periods varied from five days to ten months. The prothrombin level of the blood was decreased to less than fifty per cent of normal within thirty-six hours in more than eighty per cent. After withdrawal of the drug the prothrombin time again returned to more than fifty per cent of normal within thirty-six hours. No toxic effects were observed. 17

ANTIHISTAMINICS

Neovacagen No attempt will be made in this review to list the myriad of antihistaminic cold preparations since they are all minor variations of one basic type. However, there is one now available which employs a somewhat different principle. This product combines in one tablet an antihistaminic, methapyrilene hydrochloride (25 mg.). and the soluble antigenic substances of approximately 100, 000 million bacteria usually associated with infections of the respiratory tract. It is recommended for the stimulation of specific immunity against secondary bacterial invaders in respiratory infections. Not only is this tablet claimed to be of value against the organisms causing the distress in later stages of the common cold but also for preventing the more serious complications which often follow upper respiratory infections.18

ANTI-INFECTIVES

Benemid Research has been directed toward a search for an agent which would enhance the concentration of PAS in plasma. A substance, knwn chemically as 4' - carboxy phenylmethanesulfonanilide, which is used to enhance the action of penicillin, was tried with PAS. It was found that this chemical also inhibits tubular excretion of PAS in doing so the renal clearances of PAS are reduced to the glomerular filtration rate. Following this it was also suggested that the same

elevated concentrations in the plasma might be achieved by having PAS in a conjugated form when it reaches the kidneys so that the renal tubules would not clear it so readily. This theory was based upon the fact that 4'-carboxyphenylmethanesulfonanilide acts upon an enzymatic conjugase system.

Recently a new chemical, p-(di-n-propylsulfamyl) benzoic acid, has been shown to affect an enzymatic conjugation system which is believed to be related to the inhibition of excretion of penicillin and p-aminohippurate. Consequently this compound was tested for its effects on PAS as well.

Known as probenecid this new chemical is a stable, crystalline white powder nearly insoluble in water. At first the drug is tasteless but some have observed a bitter taste followed by a pleasant aftertaste. It can be given orally since it is absorbed rapidly from the gastrointestinal tract. Plasma concentrations have been observed for as long as 56 hours following one oral dose given to dogs. The plasma proteins bind almost 75 per cent of probenecid. It is excreted almost wholly in a conjugated form (probably a glucuronide) in the urine. A high therapeutic index was revealed by acute and chronic toxicity tests in mice and dogs. No toxicity in humans has been observed after 3 weeks' administration of the drug.

Clinical studies revealed that if given in adequate amounts probenecid will enhance the effects of PAS. Probenecid is believed to inhibit the conjugation of PAS so that it reaches the kidney in a form which is not so rapidly excreted as are the various conjugates of PAS. It is hoped that this compound will aid in increasing the use and efficiency of PAS in the therapy of tuberculosis.¹⁹

Camequin Amodiaquin, known chemically as 4(3'diethylaminomethyl-hydroxanilino)-7chloroquinoline and supplied as the dichloride dihydrate, is a light yellow crystalline powder, available in tablets representing 0.2 Gm. of the base. It is

highly effective in the treatment of malaria. Adequate dosage results in prompt disappearance of plasmodia from the blood stream and clinical recovery from an acute attack. It is also valuable as a prophylactic suppressive against acute attacks of malaria. For adults, 3 tablets (0.6 Gm.) are usually taken as a single dose. The single dose seems to produce more favorable results than the same or even larger amounts in divided doses.²⁰

Matrasil For the treatment of pyelitis, cystitis and urethritis due to infections by Streptococcus faecalis, B. proteus, E. coli, or Ps. pyocyaneus; and for prevention of such infections following surgery of the genito-urinary tract, there is available a tablet containing 0.5 Gm. and a solution containing 30 per cent of parasulfanilamide-salicylic acid, a compound of sulfanilamide and para-aminosalicylic acid. The tablets are given orally and supplemented by irrigation of the urinary tract with neutral solutions of the sodium salt.²¹

Milibis Bismuth glycolylarsanilate has been shown to possess high amebicidal potency. Amebic dysentery was once considered to be only a tropical affliction but it is now known that it is world wide in prevalence. In the United States the disease is most prevalent in the west, and south central states. A course of therapy of the drug is usually 2 tablets (0.25 Gm.) 3 times a day for 7 days. The cure rate has been stated as being as high as 90 per cent.

Toxicity tests revealed that this drug in a daily dose of 75 mg./Kg. for five days cleared 10 hamsters of amebiasis infection. Ten times the effective dose given for five days caused no signs of toxicity in these animals, an observation in striking contrast to the toxicity of effective doses of other amebicides.²²

Nisulfazole A new sulfonamide, p-nitro-N-(2-thiazyl) benzenesulfonamide, has been used in a 10 per cent suspension in acute cases of ulcerative colitis when

sigmoidoscopic examination showed that only the rectum and lower colon were involved. The dosage employed was 1 to 2 ounces 8 to 12 times daily given rectally. When it was shown that the entire colon or more was involved 4 to 6 Gm. were administered orally each day in addition to the rectal therapy. The suspension spread well and coated the mucosal surface of the rectum and colon for a period of 2 to 6 hours. Nine patients in the active phase showed rapid improvement but I relapsed several months after treatment had been stopped and did not respond to the drug following the relapse. In most cases continuing therapy was required to maintain improvement. Of 10 patients in the active phase of the chronic stage 7 showed lasting improvement but 3 had intermittent exacerbations and remissions of varying severity. This new drug had little or no effect on 4 patients who were in the polypoid hyperplastic stage of the chronic phase. Two patients showed persistent nausea which required the discontinuation of oral therapy.

Promacetin Leprosy is another one of the many diseases which more or less defies therapy. In recent years the sulfones have been used with some success. Now another sulfone, formerly known as internal antiseptic 307, is being tested. Chemically this white crystalline compound is sodium 4,4'-diaminodiphenylsulfone-2 acetylsulfonamide.

The drug was given orally at meal times in initial dosages of 0.3—0.5 Gm. Every 2 weeks the dose was increased by this amount until a maximum of 3—4 Gm. daily was attained. No severe acute toxic symptoms were observed in the 27 patients given the drug for 16 months. Uniform and sustained improvement occurred in the lesions of the skin and mucous membranes. Lesions which had responded to sulfone therapy but had become stationary and residual showed further clearing.²³

Sodium pentachlorophenate, Copper pentachlorophenate

Schistosomiasis is considered to be the world's number three health problem following after malaria and tuberculosis. It is estimated that 115,000,000 people throughout the world are affected. In Egypt 75 to 80 per cent of the entire population is infected. The economy and production of the country are believed to be reduced by one-third as a result.

Recently, the National Institutes of Health of the United States Public Health Service reported that sodium pentachlorophenate and copper pentachlorophenate are effective as snail-killers. By ridding the affected areas of the snails it is believed that the cycle in schistosomiasis can be broken. The disease is caused by a flat, leaf-shaped worm called a fluke, which spends part of its life cycle in the body of certain fresh water snails. Humans who bathe, drink, wade or do laundry in water containing these snails or the larval form of the flukes are apt to contract the disease. The flukes produce their eggs in the human body and these eggs in turn get back into the water either directly from humans using the water or via sewage.

Excellent results with these 2 chemicals in killing snails have been reported in tests in swamps, lily ponds, roadside ditches and backwash river waters in Puerto Rico. It is believed that the chemicals will have to be applied only 1 or 2 times a year. However, further studies on this subject are being conducted in Liberia. Toxicity studies of sodium pentachlorophenate and copper pentachlorophenate have shown that they do kill catfish, guppies and eels, but not crayfish. So far as is known they do not harm humans or cattle drinking or bathing in the water.

Sulfabenamide Another new drug is being tested for its value in leprosy. Chemically it is 4-N-capro-amidobenzene-sulfon-hydroxamide (N-(p-hydroxysulfamyl-phenyl) camproamide).24

Thiodiamine In India a new drug, thiodiamine, has been extracted from the bark of the Crataeva Roxburghii tree and is being used in the therapy of cholera.

Thiosemicarbazones Recently interest has developed in an entirely new series of compounds showing value in the therapy of tuberculosis. These compounds had been investigated thoroughly in Germany and the one showing the best results, TBI/698 had already been tested clinically on approximately 7000 patients. One of the original German investigators was none other than Dr. Gerhard Domagk, Nobel Prize Winner, and the discoverer of the first sulfonamides.

In vitro tests have shown that TBI/698 inhibits the growth of the tubercle bacilli in concentrations as low as 1:200,000 or 5 micrograms per cc. Para-aminobenzoic acid does not suppress this effect as it does with the sulfones and PAS.

Tests with guinea pigs and mice showed that TBI/698 was capable of suppressing experimental tuberculosis. In a comparison on animals with PAS it was found that TBI/698 required only 1/50 of the dose to exert a comparable effect.

Believed to have a primary effect upon the tubercle bacillus this compound not only inhibits the growth but it also produces morphologic alterations in the bacillus such as abnormal size and granular degeneration, formation of thread-like and coccoid forms and impaired ability to take acid-fast stains.

Studies of absorption and excretion of chemically similar thiosemicarbazones have shown that they are rapidly absorbed into the blood stream after oral administration. Within one hour after ingestion the serum concentration attains a maximum. Since only traces are observed in the urine most of the drug is believed to be destroyed in the body.

As with the other antitubercular drugs TBI/698 is to be used alone or in combination with other agents such as streptomycin, dihydrostreptomycin or PAS. In the German clinical trials it has been found effective in laryngeal and intestinal tuberculosis, in lupus vulgaris, in pulmonary and genito-urinary tuberculosis, and in tuberculous empyema. Somewhat encouraging results have been found in bone and joint tuberculosis. In miliary and meningeal tuberculosis it has shown poor results. Consequently, in these conditions streptomycin remains the drug of choice. However, TBI/698 may be administered in addition to parenteral and intrathecal administration of streptomycin.

Experiments have shown that TBI/698 may have value in delaying the development of resistance by the bacilli.

TBI/698 can be administered for a considerable length of time which may make it of value in the preparation of patients for operations, thus reducing the danger of post-operative complications. This property also may make it of value in treating chronic types of tuberculosis in which streptomycin or dihydrostreptomycin are contraindicated. Recommended doses are as follows:

ADULTS

1st week,

50 mg. orally, per day, in divided doses 2nd week,

100 mg. orally, per day, in divided doses Then,

200 mg. orally, per day, in divided doses

CHILDREN

1st week,
0.5 mg./Kg. of body wt., daily
2nd week,
1.0 mg./Kg. of body wt., daily
Then,
2.0 mg./Kg. of body wt., daily

The dosages as recommended in the table are set up with the purpose in mind of keeping any accompanying gastro-intestinal distress at a minimum. In the very beginning of therapy there may be nausea, anorexia and occasionally vomit-most commonly is found to be alcohol, ing but such symptoms usually subside (Vol. 79, No. 1) JANUARY 1951

rather quickly even though therapy is continued. These side effects also may be reduced or eliminated by giving the drug with meals and also administering small quantities of barbiturates. Antacids and antihistaminics also may be helpful.

The daily dose may be given at one time or it may be administered in 2 or 4 divided doses. Because it is not essential to maintain constant serum concentrations of the drug, around-the-clock administration is not required.

Although TBI/698 is generally given orally it can be administered in other forms. For empyema cavities, large lung cavities and draining fistulae a suspension of 10 to 20 per cent of the powdered drug in distilled water or sterile saline may be instilled in 1—2 cc. quantities. The powdered drug may be administered by insufflation into the larynx and bronchial tree.

Viacutan Dinaphthalene methane silver disulfonate in 1 per cent aqueous solution with a pH of 4.5—5 is being marketed for the treatment of trichomoniasis. It contains a wetting agent to assist spreading and a water-soluble yellow dye to indicate the areas treated.²⁵

ANTISEPTICS

Bactine A new antiseptic, bactericide, cleanser-deodorant and fungicide has been made available, the active ingredients of which are di-isobutyl cresoxy ethoxy ethyl dimethyl benzyl ammonium chloride, polyethylene glycol mono-iso-octyl phenyl ether, chlorothymol, and alcohol 4 per cent. This product is a clear, colorless, non-staining liquid with a clean, fresh odor and can be used as a general antiseptic for office, hospital, personal and home use.²⁶

lodine Solution Iodine has been established for many years as an efficient and versatile antiseptic. The solvent for the iodine has varied over the years but most commonly is found to be in alcohol, water or a combination of the two. How-

ever, the use of alcohol causes irritation and pain when the antiseptic solution is applied to open wounds. On the other hand, an increase in the proportion of water increases the hazard of freezing of the solution under conditions of low temperature storage or shipping, a hazard manifested by the damage to surrounding materials should the bottles of solution freeze and crack.

Recently Gershenfeld and Witlin suggested a solution of iodine composed of 2 per cent iodine, 2.4 per cent sodium iodide, 25 per cent propylene glycol and distilled water. This solution has a high bactericidal efficiency, a free iodine content equivalent to the present-day iodine tincture, a low freezing point, and it does not sting nor irritate the skin. It also has a desirable adhesiveness to human skin and mucous membranes.

Oronite Quaternary ATM-50 N-alkylbenzyl-N, H, N-trimethylammonium chloride is a surface-active agent and a germicide. A 50 per cent aqueous solution is nearly colorless and odorless. Determined by the modified F. D. A. method for germicidal activity, the phenol coefficient is approximately 250 (100 per cent basis). As a cationic surface-active agent it has a very high activity, reducing the surface tension of water to 38.5 dynes per cm. at 0.001 per cent concentration and 29.2 dynes per cm. at 0.01 per cent. N-alkylbenzyl-N, N, N-trimethylammonium chloride is non-toxic and non-irritating to the skin and is compatible with most nonionic surface-active agents and with inorganic salts, thus allowing for the preparation of various dry free-flowing detergent sanitizer compounds.27

(To be continued next month)

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1. Under investigation as SY-2 by Parke, Davis and Co., Inc.

2. Available as Nisentil from Hoffmann-LaRoche,

Inc.

3. Under investigation as Subdamine by Lederle
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4. Procaine derivatives are being studied by the
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5. Under investigation as Surital Sodium by Parke,

5. Under investigation as Surital Sodium by Parke, Davis and Co., Inc.
6. Fungicidin is under investigation by the Division of Laboratories and Research of the New York State Department of Health.
7. Lupulen is being studied at the University of California Medical Service, San Francisco Hospital, San Francisco Department of Public Health and the Div. of Pharmacology and Experimental Therapeutics, Univ. of California Med. School, San Francisco, Calif. under a grant from Eli Lilly and Co.
8. Thiolutin is under investigation by Charles Pfizer and Co., Inc.

Calif, under a grant from Eli Lilly and Co.

8. Thiolutin is under investigation by Charles Pfizer and Co., Inc.

9. Pentracin, a combination of penicillin and bacitracin, will be marketed by C. S. C. Pharmaceuticals, Division of Commercial Solvents Corporation.

10. Combiotic, a combination of penicillin and dihydrostreptomycin, is being marketed by Charles Pfizer and Co., Inc.; Penicillin S-R with Dihydrostreptomycin is available from Parke, Davis and Co.

10a. A combination of dihydrostreptomycin and sodium para-aminosalicylate is available for investigational use only from Para-Amino Corporation.

11. Pentresamide by Sharp and Dohme, Eskacillin-Sulfas by Smith, Kline and French Laboratories, Nectrizine by Eli Lilly and Co., Dram Cillin with Triple Sulfonamides by White Laboratories, Inc.

12. A combination of penicillin, sulfadiazine, sulfamerazine and calcium carbonate under the name Biosulfa is available from the Upiohn Co.

13. Terramycin is available in troches, capsules and in an elixir (Terrabon) for oral use; in an injectable form for intravenous use; in a dry mixture for preparation of an eye drop; in an ophthalmic olament; and in an ointment form for topical administration.

14. Thrombodent Dental Cones are available from Sharp and Dohme, Inc.

15. Vionvicin is under investigation by Charles

14. Thrombodent Dental Cones are available from Sharp and Dohme, Inc.
15. Viornycin is under investigation by Charles Pfizer and Co., Inc.
16. Under the tradename of Danilone this is being investigated by Charles Frosst Co. of Canada.
17. Available as Tromexan from Geigy Co., Inc.
18. Neovacagen is available from Sharp and

Dohme, Inc.

19. Benemid is under investigation by Sharp and Dohme, Inc.

20. Marketed as Camoquin by Parke, Davis and

20. Marketeu as Matrasil from Ward, Benkinsop and Co., Ltd. of England, 22. Available as Milibis from Winthrop-Stearns,

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23. Fromacerin is being investigated by Faire, Davis and Co., Inc., 24. Sulfabenamide is under investigation by Sharp and Dohme, Inc., 25. Known as Viacutan this is available in England. 26. Bactine is being marketed by Miles Laboration Labor

tories, Inc. 27. Oronite Quaternary ATM-50 is marketed by the Oronite Chemical Co.



Meetings and Conventions

The national convention of the American Academy of General Practice will be held in San Francisco from March 19 to 22, 1951.

Aureomycin Used to Prevent Tooth Extraction Infections

Successful use of aureomycin in reducing bacterial invasion of the blood as a result of tooth extraction is reported by a group of doctors and medical researchers at the Hospital of St. Raphael, New Haven, Conn.

Some Remarks About Psychotherapy

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Although we have advanced far, there are too many doubts concerning psychoanalytic procedures and results. In a simple form, everyone psychoanalyzes his friends, enemies, customers, children and other relations. The weight given to specific statements and actions and their interpretations varies with each analyst, lay or professional. Each, according to his education, experiences and all other training in life, has his own reception, perception and judgment about a given set of circumstances. It is well known that abstract opinions are never of the same worth as concrete performances. For instance, it is so easy to say, "If I had built that bridge, I would not have done it that way"; or, "Why didn't they put the houses on that corner," or, "Make the handle of the automobile like this," etc. If the purveyor of these abstract ideas should try to carry them out, he soon would learn how difficult the problem at hand is and how impractical his ideas are.

The school of hard knocks has advantages but it is usually too slow in our modern world. Experiences of others must be used to their fullest extent. This is one reason why students with good teachers make better and faster progress than those of equal intelligence who get their learning from books alone. Many of the greatest musicians and painters are eager to let the world know who their teachers were. The same is true of leading professional and business men. Even in

matters regarded as lowly, as the cook, the seamstress, the carpenter or the auto mechanic will state, "I have been trained by so-and-so." The stenographer will explain she formerly worked for a certain publishing outfit who insisted on doing things a certain way. This reasoning applies to all matters, serious or frivolous, good or evil. Criminals are trained not only in their technique of crime but also in the methods of eluding punishment. Thus, it is understandable how one's thoughts are the results of a gradual development from a past different in each individual.

If an analyst wants to make a success of classical psychoanalysis, he must be psychoanalyzed himself so that his interpretations are not too biased by his own feelings. He must not see life through colored glasses and, if he does, he must make the proper correction.

Psychotherapy includes a wide field—hypnosis, drugs, electric and chemical shock, institutional management, etc. are only a few which are not psychoanalytic. At times, a combination of modalities brings the best results. Even psychoanalysis is not governed by hard and fast rules. It has its variants as to length of time and intensity of treatment. A particular form of psychotherapy which may bring success in one patient may not succeed when another analyst uses exactly the same procedure. The trite question, "What has she got that I have not got?" is a popular way of showing the variations

of personalities. The relationship between patients and their analysts explains why similar results can be obtained by what appear like entirely different methods. As noted before, in a given case, the same procedural practice may give varying results when employed by another analyst.

Two sisters and a brother worked for the United States Government. They tried to keep from each other the fact that their loyalty was being investigated by the F.B. I. Each one worked in an office where some questionable persons had been discharged and others prosecuted. One sister worked in the office where Ruth Coplon was employed. These people were really liberals; their family had changed its name in the previous generation; they were originally of Russian extraction.

In the course of time, all three developed paranoid ideas that they were being looked at askance by the other employees. One of the daughters came to this office with her husband but did not tell the entire story. The family doctor was sure that she had paranoid praecox reactions. She was given a dozen electric shock treatments and made a very nice adjustment for a few months; then she broke down again when a new investigation was carried on together with Congressional debates. She is now in a State hospital,

Her sister, unmarried, was a stenographer in a Washington Bureau. She slowly developed similar symptoms, joined the Christian Science Church, achieved some peace of mind but never got well. She kept repeating "It is God's will and God does what is right." She is now in a private sanatorium.

The brother (whose wife is the sister of a physician) was taken in hand by this physician, who was with him practically every day, and took him to a well known psychoanalyst. He finally broke down and is in a State hospital in a different State.

If one of these had succeeded in freely baring his or her conflicts, not only to the therapist but to a sister or brother, it is possible that all three conditions could have been alleviated by the same therapist. Actually, they came too late, they told three different stories and had three different approaches to their psychological disorders and were unable to realize that they had the same illness. At this writing, these patients are still unrecovered.

A dominant father had three daughters and a wife who acted as slaves. The two older daughters fell into the wife's pattern but the youngest daughter, bright and good-looking, revolted. The older daughters came home early, nights, while the younger one stayed out. The older daughters were Orthodox Jewesses, while the younger one was anti-religious. The older daughters gave all their earnings to the father. If they bought clothes, the mother would go with them. If they met young men, the approval of the family was sought. All three girls had responsible positions.

After two or three wild episodes, the voungest daughter was interrogated by the father and an antipathy developed between them. She finally ran away from home. Her debauchery increased, a feeling of guilt grew, sleepless nights and inefficient work were followed by the loss of a job and the girl returned home. The mother's feeling toward this daughter became more antagonistic than the father's and the girl began to feel like an unwanted child. She went into a deep depression. She required electric shock treatments. The mother would bring her to the office and, after a time, she too went into a depression, feeling guilty for what she had done to the daughter.

One sister, who had constantly fought with the youngest, succeeded in instigating the mother and the father against this daughter. Finally, she also broke down and went into a similar depression. After twenty electric shock treatments, she was restored.

The mother was given a series of electric shock treatments and the oldest sister began to worry and had sleepless nights for her part in what she thought was making the mother sick. The situation became too involved for the father and the other sister so the mother was sent to a State hospital. The entire family went to see her and the youngest daughter, who was now restored to health, thought she was responsible for the mother's condition and broke down again. They are now both in a State hospital. The other daughter has been given electric shock treatments and is well since several months.

These two cases are cited to illustrate that whatever form of therapy is used, no permanent results can be achieved unless the entire families and the environments are corrected. The various forms of psychotherapy could mitigate the symptoms of the individuals or even remove them but, unless the entire picture is presented, the therapy cannot produce permanent recovery.

An epileptic man of forty-four takes a defeatist attitude toward society. His decrepit old mother pities him and by doing so stimulates his negative thinking. He feels he is not even a man any more, that he is turning into a woman. When he tells that to his mother, she gives him all the sympathy of which she is capable and he gets worse. The other children love their mother and sympathize with her. This, in turn, stimulates the mother to intensify her feelings toward her son. The result is, our patient feels he cannot work any more; that people look at him and talk about him. Although he has been an epileptic, his delusions have been more of a nuisance than his seizures. He has had thirteen electric shocks and his delusions have disappeared but the sympathy of the mother prevents him from working, and further delusions may be expected. How can any form of therapy aid this man unless the mother is treated? It is a form of delusion of the mother to believe (and express her belief) that the son cannot ever win the battle of life.

A divorced woman of fifty who has had more of the world's goods than most of us, but has not had sufficient schooling or encouragement to develop her mentality, became restless. Some of her friends introduced her to a religious sect—as a pastime—to get her interest. She liked it and felt some of her restlessness and lonesomeness disappearing. She has now developed a delusional trend of a spiritual nature. When she hears of a death or sees an accident, no matter how serious, she says with a smile, "It is God's will, He knows what is best, we do not understand."

Whether the treatment be religious, or classical psychoanalysis, or drug therapy, or physiological therapy, the symptoms will be relieved so long as the patient is interested enough in cooperating and has faith enough in the results. Actually, a transference of her first symptoms takes place, and the patient is really not cured at all but a new set of symptoms of the old illness is established. Even careful, long-drawn-out analyses might succeed in making this patient understand the situation but that would not necessarily cure her. A useful and agreeable transference of her symptoms is indicated but it must be agreeable and her loneliness should be ended. "Agreeable" is one of the most important points to emphasize; the patient must like the therapy employed.

Individuals have many psychoses or neuroses which are kept dormant by their own effort; or, there may be no reason for displaying them. Any serious illness, accident, grief or other emotional disruption of one's equanimity will remove the equilibrium and a full-fledged patient is presented. In other words, many psychotics become adjusted to their environment; that is how they are discharged from hospitals and anything that will interfere with their adjustment permits the psychoses to return to the fore.

The transition from normal or average thinking to a delusional state is gradual; and mild delusions are often unrecognized. The propriety of nudism, the tenets of some religions, the chauvinism of some governments, certain reactions to food, sometimes give rise to mild delusions. Attention is directed toward these delusional states when they interfere with other people's everyday pursuits. The popular "honi soit qui mal y pense" is one interpretation of delusional conceptions and individual reaction to such a concept varies not only as to its propriety but also as to its pathological significance.

Four essential things for success in psychotherapy are:

- 1; the experience and ability of the therapist.
- 2; the rapport between patient and therapist.
- 3; the agreeability, the hope, the cooperation and desire of the patient to be in the hands of a particular therapist.
- 4; the nature of the therapy must be within the mental grasp of the patient; the patient must understand what it is all about and be able easily to fulfill the directives.

It is easy to conceive why different patients, even with the same set of symptoms, will recover through various psychological processes. Religion, metaphysics, medical psychotherapy, drugs, or change of environment may bring good results; but the varied psychology is not in what was done but in the ego of the patient; that is, how the patient himself reacts to the therapy. This is not a willful, conscious behavioristic matter but a subconscious, uncontrolled reaction. The more one works

with psychiatric problems, the more important does the unconscious sphere become.

A married woman had a love affair ten years before she met her husband. This was a one-sided affair-the man with whom she was in love hardly knew her. She developed an intense libido. The object of her affection married someone else and moved two thousand miles away, and eventually had a family. Ten years later, our patient, who married at twenty-five, could not shake her feelings for her first love. Mentally, physically and financially, her own husband had much more to offer than the first man, and she knew it. But, she was continually annoved with the mental and emotional conflict between thoughts of her previous lover and her husband; so much so that she became inefficient and lost much weight. trembled and had peculiar vasomotor disturbances and occasionally remained mute for a day or two.

This case requires no detailed analysis to explain her situation. Two different psychiatrists gave her electric shock treatments hoping, thereby, to cause an amnesia. The result was good for from two days to two weeks and then everything returned again. She confessed to a priest and he worked with her religiously without results.

We told her to write her story to the wife of the first lover. Previous to that, we had written to the wife explaining the story and had her tell her husband all about it. Both of them subsequently wrote to the patient as recommended. The man did not even remember what she looked like after so many years. He now had a family and thought she was ridiculous in her behavior. As far as he was concerned, there was nothing between them. Later, a second discouraging letter enabled our patient gradually to adjust herself. Her husband knows all about the situation and there has developed a

new affection between the two. When this woman is seen today, it is unbelievable to think of how she was until a year ago.

Another case where a particular type of psychotherapy was used is about a woman of fifty who had had a love affair for twenty-five years. The man belonged to a different religious group and came from an entirely different cultural class of society. He made all the customary excuses why he would not marry the lady, saying, (1) he had to support his mother: (2) while she was living, he would not marry outside of his religion; (3) he did not make enough money, etc. He said these things so often that he believed them himself. But, whenever our patient did not see him for a week or ten days, he would annoy her until the affair was renewed.

Both her friends and his friends were cognizant of the situation. They frequently appeared together at social functions and he never took another lady out and she never went out socially with another gentleman. They agreed, if either one found another more interesting, he or she would not stand in the way. Social workers and psychiatrists were consulted by each one on a number of occasions. Sometimes promises were made but were not kept. The lady was advised to go on a cruise. The hostess of the cruise was notified of the situation and succeeded in having another gentleman pay amorous attention to our patient. They are now married and live happily in Philadelphia. To say that this woman had only conscious and not unconscious emotional conflict is not exactly true. Consciously, with her will, she realized the futility of the first affair and tried many times to break it up, but found that impossible. When a transference took place, the result was easily effected.

A case of gastric ulcer, which had been operated on, in a man of fifty, recurred.

He was an unsuccessful professional man, but although his income was never large, he never suffered financial or social poverty. It was suggested to him many times that he change his profession or take on some sort of a position. His pride would not allow him to do it and his unhappiness increased.

He became interested in the American Legion and joined their glee club and bowling groups and made himself popular there. He finally was appointed Official Delegate of the National Group. He now holds a national position for which he is paid a salary. Although he still maintains his office, he throws out his chest and considers himself a successful attorney. His time is so much taken up with the Legion affairs that his professional income has dwindled. His ulcer has disappeared, he has gained pounds in weight, he sleeps well, he is happy and, with about the same income, he acts like a successful lawyer. His emotional reaction is below the conscious level because this man always was popular socially and his material status is unchanged. Even his dress is different than it used to be.

There are times when encouraging a patient requires special sophistry. A philosophical discourse may be necessary to make the patient understand the reason for the encouragement or why the patient will get well and why the particular patient is different than other people and must get well. The technique used may be repetitious but if the patient believes in the therapist, who is hammering away to get certain results, and the patient is anxious to recover, he finally becomes sympathetic, cooperates and recovers. In other words, there will be full cooperation, both conscious and unconscious, and a poor prognosis will be changed to a good one. The patient becomes enthusiastic and has even more faith in the doctor than he had before. He has a new perspective and new enthusiasm. This procedure has cleared up many cases quickly and permanently.

Psychoanalysts know well that no single form of therapy fits every case. Even in the progress of an analysis, it may be necessary to switch from one form of therapy to another. Symbolism, memories, conflicts, complexes are subdued or overcome entirely by the majority of people. In the course of a lifetime, we are all affected by these things and it is only when we cannot manage them or when they pervert our normal activities and we are hampered from proper living that professional assistance is necessary. Even if we do not know the exact origin of the disorder, it is often possible to circumvent it and life may be adjusted to most situations. In orphan asylums, in grade schools, high schools, colleges, homes for the aged, etc., there are always present such conscious and unconscious irregular situations. Although the psychic processes are quite well understood nevertheless there are an endless number of cases for which the most advisable therapy cannot be determined without trial-anderror methods. We have all seen cases of long standing suddenly recover without any treatment whatsoever and the reverse is also true. What made them recover was a psychotherapeutic impulse administered without intent. Physiological and psychological therapy go hand-inhand. For this reason, often, physiological results are achieved. The patient does not realize that the physiological procedure is really directed toward a psychological cure. Many so-called electric belts, various electric modalities which are employed, some forms of physical therapy and even some drugs can thus produce a psychological effect. The conscious mind is directed toward the therapeutic agent and permits the subconscious to become more dormant. Then the conscious rules the subconscious and the symptoms are ameliorated or made to

disappear entirely.

It is not always possible for a patient to use his will power to overcome a subconscious annoyance, and then a conflict develops between the conscious and the subconscious. If, at this point, an acceptable physiological agent is used adequately to occupy the patient mentally, the subconscious will be quasi-overpowered and thus the symptoms will be removed.

Individuals differ in the qualities of their subconscious. What one would accept favorably as a curative agent for his symptoms will differ from the kind of therapy which is desired by someone else. Although the psychological process of recovery is the same, there is no question that a psychological approach will work with one, and a physiological approach may be necessary for another case. It is here that the various cults, religious and otherwise, are so valuable to a particular patient.

The psychoanalyst produces results in two ways: (1) The patient gets better because he feels he is being studied, his symptoms are carefully weighed, understood and explained; (2) The patient is aided in discovering the origin of his disorder and the sequence of events which led up to his present group of symptoms. Attempts are made to evaluate and adjust each one of these.

The sum total of all our experiences varies and grows with every person, and each one is unique. This is true of the analyst as well as the patient. Regardless of these variations, with long clinical experience, careful diagnosis and proper therapy, recoveries take place. Witness the new psychosurgery, the electric and chemical shocks, etc., with their combined psychological and physiological results.

Explanations of psychological functions are being substituted by physiological and organic facts instead of metaphysical and mystic reasoning.

The evaluation of the modus operandi,

individual or psychodrama therapy, in the last analysis, is really individualistic. This is true because behavior and reactions are individual no matter what the origin, be it group such as state, church, family or gang, or be it just another single person. Of course, some of us are more susceptible to suggestion than others and the more suggestible the patient, the easier he is to cure.

A twenty-two year old male, who was a lieutenant in World War II, was told by a nurse and an orderly in the sickbay of a boat that when he landed in France he would lose weight, suffer from indigestion and become very nervous. The reason given was that his eyes showed the lack of a certain mineral in his system. Doubt was put into his mind and shortly after he reached his destination. he went to a hospital, related what he had heard, and it was explained to him that this was not true. He tried to believe what they told him, but still he lost weight from lack of appetite and became nervous from loss of weight. His normal weight was one hundred thirty pounds and he went down to ninety-eight pounds. After two months, he was sent home. He never reached weight of over one hundred pounds even after he was home, until four years later a social worker in the Veterans Hospital got in touch with the nurse who had first suggested the loss of weight to him. She told him it was only a hoax and, after two weeks during which he saw the nurse three times, his symptoms gradually disappeared. He now weighs one hundred fifty pounds, is married and has two children and is apparently well. A number of various forms of psychotherapy were used on this young patient, without appreciable results, until a short psychoanalysis brought the origin to light and removed the cause.

There are times when electric-shock therapy or insulin or sodium amytal injections remove some inhibitions and the patient talks freely with the therapist. With such a lead, treatment is easier.

A forty-five-year-old painter, happily married, having three children, was out of work. He left home one morning to seek employment, disappeared, and the family did not hear from him for three years. One day, in Cook County Hospital in Chicago, he told the authorities his name and address in Brooklyn. From then on, he was apparently well and was sent home and went back to work. He had no idea about his fugue but he did develop a psychoneurosis based on what had happened to him in all this time. After a few visits, hypnosis was tried. While in the trance, he told his whole story. He said he went out that morning but could find no work. Then he went to a pawnshop and pawned an old watch and chain. With the money, he went to Chicago and tried to get work there. He wanted to run away from all the trouble in New York and start over again. He did not get work in Chicago, was exhausted and fell asleep. He was picked up by a policeman and taken to the Cook County Hospital, where he remained for three years. He never knew his name nor his home address. In fact, he did not know he was in a hospital. He was quiet, took his food well and then did whatever he was told. One night, he had a dream. He dreamed he was home and his wife asked him where he was. He awoke from this dream and then told the authorities his name and address.

The hypnosis took place a year after he was discharged from the Chicago hospital. During this year, he was nervous, he had sleepless nights and was annoyed very much trying to find out why and how he got to the hospital. After he awoke, the whole story was explained to him and now this man is apparently entirely well. He was given sodium amytal at the hospital and they had tried electroshock without results. Actually, the sub-

conscious drove him away from everything. The hypnosis was a means of getting in contact with the subconscious.

Hysterical fugues are common enough but actually they do not last so long. An attempt has been made to clarify the management of some of the usual cases that are placed before the psychiatrist. Over simplification may have been the result.

An effort has been made to emphasize:

- 1. The individuality of each case.
- 2. The individual personality of each

therapist.

- 3. Different forms of psychotherapy.
- The same cause may affect different psyches in different ways, and this is true of the therapist, patient and modality.

Finally, this is an explanation of why a patient will do better with a particular therapist or a particular type of treatment. There is no special therapy for every case and it often takes a number of changes of therapists before one is found who is most suitable for a particular individual.

502 Washington Avenue.

A New Nobel-Prize Winner from Zurich

Professor Thadeus Reichstein, born 1897, who has been awarded the Nobel-Prize for physiology and medicine together with Professor Hench and Doctor

E. C. Kendall of the Mayo Foundation in Rochester (Wisconsin), is a citizen of the city of Zurich, Switzerland. The mentioned Nobel Prize has been awarded in common to these three scholars for their discoveries concerning the hormones of the cortex of the suprarenal gland. Independently of each other they discovered this summer, approximately at the same time, the hormone cortisone which injected in

the human body brings health back to those suffering from rheumatism, arthritis and other painful illnesses.

Professor Reichstein originally had headed for engineering, but changing his mind, he entered the Swiss Federal Institute of Technology in Zurich to study chemistry and graduated there as doctor of chemistry. In 1929 he became him-



Thadeus Reichstein

self professor at this world-famous school and collaborated as assistant with Professor L. Ruzicka, another Nobel Prizewinner of Zurich. At this time Professor Reichstein made himself a name by effecting the chemical synthesis of vitamin

C. In 1937 he was appointed as extraordinary professor for organic chemistry at the Swiss Federal Institute of Technology and received subsequently a call to the University of Basle (Switzerland) where he has been lecturing ever since. The highest scientific recognition received by Professor Reichstein is not only an honor for himself and the University of Basle, but also for the city of Zurich.

To date no fewer than eight members of the Swiss Federal Institute of Technology or the University of Zurich have been winners of the Nobel Prizes. This fact alone demonstrates the high level of scientific research attained in these institutions and indicates why they are centers of attraction for so many students the world over.

Hypometabolism

Its Influence on the Growth of Cancer

JOSEPH LEVY, M.D., F.A.C.P. New Rochelle, N. Y.

The problem of cancer can be considered in two parts-(1) initiation or start of the cancer cell; (2) growth of these cells in situ and in other parts of the organism. A great deal of study has been done on the factors responsible for the presence of tumor cells in various forms of life. Many theories have been developed on the basis of these studies. Yet, very little progress has been made to a fundamental understanding of the problem because the initiation of cancer cells is intimately related to the concept of life itself. Until more is known concerning the difference between animate and inanimate matter, little can be gained from the study of how cancer cells begin. On the other hand a great deal is known about the growth of cancer cells. Many studies have been directed to influence the growth of these cells as well as to eradicate them. The object of this report is to summarize work done in biology, chemistry, physics and experimental medicine to show that by influencing the metabolism of the organism in which the cancer is growing. direct and indirect effects on the cancer cells can be produced. Much of this evidence at first glance appears to be paradoxical because of the multiplicity of the factors that enter when one considers controlling the environment of an organism as a whole and cancer cells in particular.4,17

Considering the differences that occur when cancer is present in a young organism and in an old organism, it is found

that the brutal, aggressively metastasizing cancer in the young rarely occurs in the aged. It is the slow growing cancer, the localized cancer, that afflicts the aged. In fact, older individuals may harbor and survive multiple neoplasms. In a review of 216 successive neoplastic autopsies, it was found that the incidence of multiple neoplasms was about eleven times that expected to occur. In a total of 16 patients with multiple cancer there were 7 cases in the age group 65-81.13 Metabolic studies have shown that there is a great difference between the young and the aged. Youthful organisms and young tissues have a high metabolism while old organisms and aged tissues have a low metabolism. The work of biochemists and radiophysicists indicates that there is a humoral factor which is important in the continued growth of a cancer.11 One cannot help but feel that the humoral factors which are responsible for the low metabolism of the aged are the very factors which prevent the aged from developing wildly growing metastasizing cancers and which limit the growth of new tissue to relatively slow growing cancers. Though the tumors that are present in the aged are all present in the young, there are antagonistic factors present in the aged that limit the growth of these tumors.

With these thoughts in mind, it is necessary to consider the factors that reduce the virulence or the rate of growth of a cancer. This could be accomplished by reproducing the conditions in the young

that are present in the aged. Thus it may be possible to make an atypical growth stationary instead of permitting it to grow. It is well to remember that a stationary tumor in a live organism is less harmful than a wildly growing tumor in the same organism.

In a review of the methods which heretofore have been employed in stopping the growth of cancer, the best method is to discover a stationary tumor before it begins to break out of its limits and remove it. Such complete excision of a growth is the ideal method of stopping a cancer. If this could be accomplished with every known type of new growth there would be no need for the present studies. Since this can be accomplished rarely, it is important to consider other methods for the control of cancer.

Following the discovery of the x-ray and radioactive substances, special tools could be employed to stop the growth of cancer. With the use of such well established methods, i, e., surgery and irradiation, one can cure selected types of cancer. The effects of x-ray therapy and radioactivity not only involve the actual destruction of the tumor and non-tumor tissue but also depress the metabolic activity of the particular tumor and the organism as a whole. It has been shown in vitro and in vivo that radiation slows down the oxidation requirements of tissue.1 In other words it creates a state of lowered metabolism of all cells.

More than a decade ago, there was a great deal of work done on refrigeration as a method of controlling cancer tissue. 12 Many experiments have shown that refrigeration causes hypometabolism. 7.8 Thus the beneficial effects on cancerous growths were accomplished by lowering the metabolism of the organism. However, this method was not found to be practical for the control of cancer.

During the past few years, study has been directed toward the effect of diet on the development and growth of cancer.²

It has been found by many workers that a reduction of caloric intake of mice reduced the rate of growth of tumors.18,19 It did not matter what type of tumor it was tried on; induced and spontaneous sarcoma growth rates were reduced by underfeeding and strict caloric restriction. Experiments on protein-deficient and vitamin-deficient diets showed that the two had little or no effect on tumor growth. Lowering the food intake of an organism lowers the metabolism and while in this state of lowered metabolism, the growth of neoplastic tissue is retarded. Analyses of insurance records have shown that in the distribution of cancer mortality according to absolute weight of people, individuals who are definitely underweight have a lower cancer death rate than those who are overweight.10 Correlating these statistics with the underfeeding experiments on laboratory animals, a definite relationship between the lowered metabolism accompaning undernutrition and the reduction of cancer growth is suggested.

Another valuable line of investigation is the type directed to the study of the occurrence of growing cancers in the many systemic conditions giving rise to hypometabolism. The outstanding clinical condition which produces hypometabolism is hypothyroidism. In patients suffering from hypothyroidism, there is a scarcity of people who have growing cancer. Thus in a 20-year study of 262 cases of long standing myxedema, only one case in the series died from cancer. An analysis of this case showed that the cancer had developed after the patient had been given thyroid extract for more than 20 years. Another clinical condition which may produce hypometabolism is a depressed activity of the other glands of internal secretion. In a review of 80 additional cases representing a depressed activity of the pituitary gland, only two cases of cancer were found. In both cases a state of lowered metabolism was treated for several years with thyroid extract.18 An ac-

complished group of investigators have shown that normal rats, after treatment with growth-hormone injections for many months, often develop tumors, whereas hypophysectomized animals subjected to the same treatment never do. This suggests that the pituitary, under appropriate stimulation, creates a cancer-producing substance. Conversely, inhibition of pituitary function prevents the liberation of this substance and limits the production and growth of tumor tissues. Another of the causes of hypometabolism is the reduced activity of the organism. This can be produced readily by the use of sedatives. It has been observed, in cases that have cancerous growths, that the use of morphine or its derivatives may extend life by inhibiting the growth of the tumor for a long time.

In view of the foregoing facts it is worth while to review artificial methods of producing states of hypometabolism in animals that have been shown to have cancer.3, 9, 15 When these cancers cannot be removed by the usual methods, a state of hypometabolism can be produced by the surgical removal of an endocrine gland or by administrating a safe chemical agent capable of specifically blocking the secretion of a single endocrine gland. The secretions of other glands will be affected. Such altering of the normal endocrine balance leads directly to multiple glandular deficiencies and indirectly to deficiencies of the many tropic hormones of the pituitary, especially the growthhormone.5 Some of the many anti-thyroid drugs, that have been introduced during the past few years, can be fed to the organism to accomplish this purpose. The least toxic and the most effective of these drugs is propylthiouracil. In a previous study, it was found that a state of well being which accompanies the hypometabolism that is produced by propylthiouracil can occur in a variety of conditions after the feeding of this drug.14 The direct inhibition of thyroid hormone and the

indirect inhibition of pituitary growthhormone by substances such as propylthiouracil cause a state of hypometabolism which, as shown by the preceding section of this review, will aid in retarding cancer growth.

- Conclusions (1) There is a definite relationship between hypometabolism and cancer.
- (2) The effect of hypometabolism is to retard the growth of neoplastic tissue and this slowing down of growth is effective in controlling the growth of cancer.
- (3) An induced state of hypometabolism, which can be accomplished through the surgical excision of an endocrine gland (thyroid) or by using an anti-hormone drug (propylthiouracil) may be helpful in controlling the growth of cancer.

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Electrocytology as Revealed by Fluorescence Microscopy

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Electrical phenomena in tissues and cells form today an important part of medical research and it is understandable therefore that research and clinical medicine evidence a great interest in the determination of the properties which influence these phenomena. Fluorescence microscopy is well adaptable to this type of research, as fluorescence being an electromagnetic phenomenon, many of its properties are

dependent on characteristic features of electricity.

The basic principles of this type of investigation differ from the usual microscopic examination and the interpretation of the findings is governed by different rules.

Fluorescence is the property possessed by a variety of substances to generate light which is different in color from the

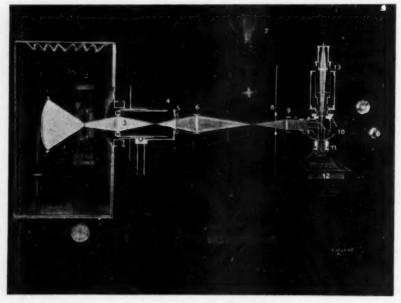


Fig. 1. The fluorescence microscope.

Table I VITAL STAINING WITH FLUORESCENT SUBSTANCES

The Decisive Factors for the Staining are the Physico-Chemical Properties of the Fluorescent Dyes and Those of the Living Tissues.

- THE PHYSICO-CHEMICAL PROPERTIES OF THE COLOR PRODUCING SUBSTANCES:
 - A. THE ELECTRIC CHARGE. Positive dyes are attracted by negative tissues and vice versa. The charge is unstable on most of the color producing substances and varies in the same electric field* according to
 - Concentration
 in diluted solutions particles are adsorbed
 by the arum ceitoids of apposits charge
 and take the charge of the ceitoid
 - pH not highly dissociated acid and alkaline Sucreacent dyes change their charge ac-cording to the electric field in which they travel
 - 3. Size of the particles in the dispersed phase phase a. cearse dispersed $0.1mm-500m_{\tilde{M}}$ b. celleid dispersed $0.00m_{\tilde{M}}-1m_{\tilde{M}}$ c. highly dispersed $1m_{\tilde{M}}$

 - B. SIZE OF THE PARTICLES IN THE DIS-PERSED PHASE² OF THE COLOR PRO-

- DUCING SUBSTANCE will influence the
- diffundibility

 C. CHEMICAL AFFINITY

 D. OXIDABILITY AND REDUCIBILITY

 E. SURFACE DYNAMIC ACTION OF THE PARTICLES
- II. THE PHYSICO-CHEMICAL PROPERTIES OF THE LIVING TISSUE:
 - A. THE ELECTRIC CHARGE. Positive tissue attracts negative dyes and vice versa
 - MECHANICAL STRUCTURE AND TRANS-MISSION density. This makes it possible or impossible for the substance to travel to different places of attraction. Difference in staining according to the manner of application. application
 - Alkaline positive will negatize the C. pH. electrically unstable fluorescent substances.

 Acid negative will positivize the electrically unstable fluorescent substances. At isoelectric point there is no staining.

VITAL STAINING IS NOT GOVERNED BY THE FOLLOWING CHARACTERISTICS OF THE COLOR PRODUCING SUBSTANCES

- ACIDITY OR ALKALINITY IN DISTILLED WATER. The relative acidity or alkalinity changes according to the isoelectric niveau of the gel membranes in the living cells. OR ALKALINITY IN DISTILLED 1.
- II. CHEMICAL CONSTITUTION. Chemically closely related substances behave differently and similarly acting substances belong to a variety of chemical groups.
 - blood serum, lymph, tissue and cell fluids secretions.
 - phase designates the parts of a substance that are separated by physical means. Dis-
- III. SOLUBILITY IN LIPOIDS. Not dissociated, non-ionized) molecules penetrate living cells easiest. Lipoids and other solvents, kaolin, charcoal, etc., with low dielectric constant seem to have a special affinity to these substances which water with high dielectric constant does not have. Lask of electric constants does not have. Lack of dissociation not lipoid solubility is impor-

persed, internal, phase is the apprepais of finely divided suspended particles in a col-loidal solution. 3. inductivity of a non-conductor.

light thrown upon them. Only a few organs of the animal body contain substances which have a characteristic fluorescence, therefore to apply fluorescence microscopy to animal tissues one has to impart fluorescence to the organs, i.e., one has to stain them by fluorescent substances. In contrast to the conventional staining methods fluorescent staining requires extremely low concentrations of the coloring substances (1:100,000 to 1:1,000,000). Due to this fact fluorescent staining of living tissues can be accomplished without damage to the experimental subject, and this extremely low concentration is also most valuable for the study of electrical properties of the tissues, as one can

apply the laws of physics without essential modifications.

The microscope for observation of fluorescence phenomena differs from the microscope used for observation in white light in that all its optical parts are constituted of material devoid of any fluorescent properties, as the fluorescence of lenses and cement used in the conventional microscope would interfere with the observation. Examination of fluorescent tissue sections and of living tissues is carried out in dark field, as in bright field the transmitted light from the monochromatic filters, which are necessary, causes effects that interfere with the fluorescence. A detailed description of the

microscope is omitted, because the apparatus has been described in previous publications, and its construction can be fully understood from figure 1.

The technique of this type of microscopy for living tissues was developed by Ellinger and Hirt² and by Singer³ and that for tissue sections was devised by Exner⁴, Haitinger⁵, von Querner⁶, and Evans and Singer.⁷

In order to obtain information about the electrical properties of the essential components of the various tissues the sections used for examination were made from fresh specimens without any fixation whenever possible. Sectioning and staining of the central nervous system presented difficulties. It was not possible to produce satisfactory frozen sections of any part of the nervous system without prior fixation in formalin. No fluorescent staining of the nervous system has been accomplished heretofore without the use of mordants. Mordants, however, change the electrical properties of the tissue, thus this method was not suitable for our purpose. The penetration of fluorescent dyes into organic matter is greatly facilitated by a high dielectric coefficient of the solvent, as shown by Singer and Nerb⁸ on bacteria. By choosing solvents with high dielectric coefficients it was possible to make fluorescent stainings without mordants. In spite of these limitations imposed upon us by the properties of the tissues of the central nervous system, the experiments showed results which are an advance upon investigations that have been carried on before and they can serve as a guide for the interpretation of the function of these parts.

In a number of prior papers an attempt was made to correlate the histological picture with the electrical potential of tissues; in this paper a further elaboration is made of the staining mechanism of tissues as having significance with respect to their electrical properties.

The interrelation between the results

of staining and the electrical properties of tissues and that of the dyes employed for the staining can be clearly discerned from Table 1.

The difference between the living cell and the lifeless environment is that in the living cell amphoteric basic dyes are mostly negatively charged and the amphoteric acid dyes are mostly positively charged, while in lifeless environment basic dyes are mostly positively charged and acids are mostly negatively charged.

For the present investigation indicator dyes were selected, which in addition have photodynamic action (they exert an influence upon the tissue, when exposed to ultraviolet radiation, and when the conditions in the tissues change the color of the dye also changes). Each dye was tested for its electrical charge against water, because the behavior of the dye particles in an electrical field cannot be predicted from their chemical composition. The filter paper test was used to determine the electrical charge. Coehn9 showed that if a substance of higher dielectric coefficient comes in contact with a substance of lower dielectric coefficient, it becomes positively charged. The substance with the lower dielectric coefficient will be negative. Filter paper, which has a low dielectric coefficient, when immersed in water becomes negatively charged. The dyes placed on filter paper showed the following behavior:

Both dyes appeared in the immersion zone in the same condition as they were in the solution. This zone was surrounded by the anode zone having a zigzaggy margin. In this zone the indicator dyes appeared in an acid color.

Negatively charged dyes: no appearance beyond anode zone. The water penetrated from the anode zone forming the colorless water zone.

Positively charged dyes: did not separate from the water at the anode zone but continued into another zone called the cathode zone, appearing there in an al-

171000 0				
Dye	Chemical constitution	Filter paper fest	Fluorescence color in acid in alkali	
phosphine O acriflavine thiazol yellow thioflavine S primulin yellow eranin esculin	acridin dye, basic acridin dye, basic thiazol dye, basic thiazol dye, basic thiazol dye, acid fluoran dye, acid glycoside, acid	in water—	greenish green bluish yellowish green blue yellow blue	yellowish yellow brown bluish

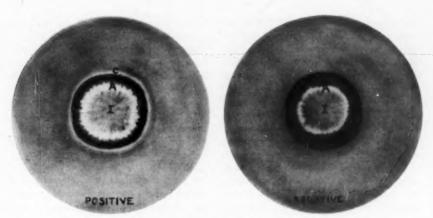


Fig. 2. Filter paper tests. C. cathode zone, W. water zone, A. anode zone,

kali color (see figure 2).

The variations in color of the dyes used in the experiments can be seen from table 2.

The description and discussion will be limited to those parts in the various organs which showed a behavior that was not apparent in the usual microscopy in white light.

Nervous System In the central nervous system the ganglion cells showed such a behavior. The ganglion cells in the different parts of the central nervous system showed consistently a quantitative difference in their staining qualities. Some stained faster and stronger, others slower and weaker. Qualitatively the results were identical in all the test objects, which included brains, spinal cords and intervertebral ganglia of rabbits, rats, and

mice.

1. The ganglion cells, when stained with Phosphine O, showed a large number of yellowish orange granuli in the cytoplasma, green mitochondria, and green nucleolus. The nucleus stained only after prolonged ultraviolet irradiation, when it appeared green. Phosphine O is a negatively charged indicator dye; it appears green at the anode, which is its acid color, and yellow is its alkali color. Electrocytologically the findings can be interpreted to the effect that the mitochondria and the nucleolus must have a strong positive charge and a large part of the cytoplasma a negative charge (See figure 3 a).

Thiazol yellow showed a number of granuli in the cytoplasma staining consistently in bluish green color. Since the





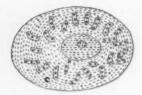


Fig. 3. Diagrammatic drawings showing a spinal ganglion cell.

Action of phosphine O.
 Action of thioflavine S.
 C.
 Diagrammatic representation of the electrocytology of the ganglion cell.

bluish green color of Thiazol vellow appears at the anode it indicates that the cytoplasma of the ganglion cells is electrocytologically not a homogenous mass but contains electropositive and electronegative elements.

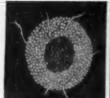
3. Thioflavine S showed the cytoplasma stained bluish, the nuclei and the mitochondria brownish. After prolonged illumination with ultraviolet light the bluish color in the cells turned brown. The bluish or cathode color of Thioflavine S indicates a negative charge in the cytoplasma and the brownish alkali color indicates a positive charge in the nucleus and mitochondria. The change in color of Thioflavine S in the cytoplasma after ultraviolet irradiation denotes a change in the composition of the cytoplasma (See figure 3 b).

The ganglion cells appear to have a strong positive pole in the mitochondria and in the nucleolus with weaker positive poles distributed throughout the nucleus and cytoplasma. In the ganglion cells are strongly oppositely charged poles in close proximity. In order to permit the existence of this condition the poles must be well insulated. Insulators are substances with low dielectric coefficient. Our model experiments, in which we varied the dielectric coefficients of solvents, gave indications that the basic substance of the ganglion cells consists of material with low dielectric coefficient. Furth10, who made measurements of the dielectric coefficient of the brain, however, found that it had a dielectric coefficient higher than

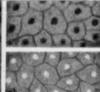
water. Since he measured the brain as a whole mass, his results must give an average figure for the entire brain substance. If the cytological findings can be correlated with the physical measurements then we must accept the concept that in the nerve tissues we have very highly conductive material, which is surrounded by good insulators. This explanation would well fit the function of the nervous tissue (See figure 3 c).

TONSIL The fluorescence staining of the tonsil revealed an electrocytological status, which the conventional staining did not make apparent. Freshly removed human tonsils served as test objects, which were examined in toto in reflected light immediately upon tonsillectomy, after a drop of 1:1,000 solution of the fluorescent substance was placed upon the mucosa or upon a cut surface.

1. Acriflavine stained the lymphoid cells in the lymph follicles yellow; the germinal centers appeared blue. This indicates that a positive charge exists in the lymphoid tissue surrounding the germinal centers, which are negatively charged. The lymph in the lymph vessels appeared yellow in very fresh tonsils. This staining appeared a few minutes after the application of the dye and lasted a short time, after which the lymph vessels lost their staining and became indiscernible. Since vellow is the alkali color of acriflavine, the phenomenon indicates that the lymph itself has a positive charge; the short duration of the staining, however, cannot be explained (See figure 4 a).







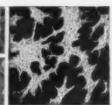


Fig. 4. Diagrammatic drawings showing the action dyes on the tonsil.

a. Acriflavine in a lymph nodule.

b. Thioflavine showing the reticulum in a lymph nodule

c. Primulin yellow in the squamous epithelium before (I) and after (2) photosensitization. d. Jranin showing trabeculi. e. Diagrammatic representation of the electro-

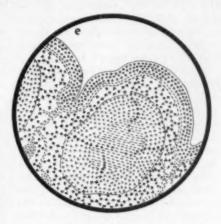
Diagrammatic representation of the electro-cytology of the tonsil.

2. Thioflavine S stained the lymph in the lymph vessels and the reticulum between the lymphatic cells light blue, indicating a positive charge for these structures (See figure 4 b).

3. Primulin yellow stained the cytoplasma of the epithelium but did not stain the lymphoid cells. After prolonged illumination the nuclei of the epithelial cells were stained, indicating a tissue interference by ultraviolet light in the presence of the dye. Since primulin yellow is an anodal dye the staining indicates a positive charge in the epithelial cells of the mucosa (See figure 4 c).

4. Uranin stained the trabeculi of the lymph follicle green. Since the green color appears at the cathode, the trabeculi would appear to be negatively charged (See figure 4 d).

The tonsil seems to be an organ having a negative charge in the connective tissue of the trabeculi but a positive charge in the connective tissue which forms the reticulum of the lymph follicles. The lymphoid cells surrounding the germinal centers have a positive charge but the cells in the germinal centers have a negative charge. The cytoplasma of the squamous cells covering the external surface of the tonsil appears overwhelmingly positive. In the tonsil closely similar tissues have opposite electrical charges,



indicating different functions for closely related structures (See figure 4 e).

Suprarenal Gland In the cortex of the suprarenal gland phenomena were observed which could be correlated to phenomena observed in white light. The tests were carried out on the living suprarenal glands of frogs, which were examined in

1. Acriflavine, a negatively charged dye, stained the nuclei, indicating a positive charge in the nuclei.

2. Esculin, a positively charged glycoside, stained the cytoplasma, indicating a negative charge in the living cytoplasma of the suprarenal gland. In the living normal cytoplasma a fine reticulum-like network appeared, however, which did not take esculin and which appeared in a brownish autofluorescence. This fine network could be observed only in the living and apparently intact gland. In white light the cells showed a granular appearance (See figure 5 a).

If some severe injury occurred to the animal, the fibers of the network, which appeared in the fluorescent staining, underwent a characteristic change. The fibers coalesced clumped together; the network disintegrated turning into brown blotches. In white light the granular appearance of the cells changed to a globular one by the coalescence of the granuli. This phenomenon occurred first in isolated parts of the gland and slowly progressed until the entire gland became thus affected (See figure 5 b and c).

These changes occurred before the blood circulation of the gland itself was affected. Thus if any damage to the cells was caused by an injurious substance, this substance must have been carried to it by the circulation. With the clumping of the network fibers esculin was released from the cells and poured over the entire gland, causing a diffuse fluorescence. This phenomenon must be an indication that the negative charge of the cytoplasma was reduced and thereby the potential difference between the dye and cell was equalized, resulting in the release of the electrically attracted oppositely charged substance.

In our staining experiments on tissue sections we used a large variety of substances (drugs), in effective blood concentrations, which have a specific effect on tissues in vivo, from which the sections were made. The changes that occurred after the application of these substances, however, depended only on the changes they caused in the pH or in the dielectric coefficient of the solvent. If the same substances were applied, however, in vivo, and the organs were observed in situ, the characteristic drug action upon the various parts of organs and that of the individual cells could be observed (Singer11). The most striking results were observed in the kidney.

Kidney The positively as well as the negatively charged normal constituents of the plasma and also the artificially introduced dyes are filtered through the glomerulus and by selective reabsorption in the tubules some of the substances become concentrated in the urine. There is, however, a small group of substances, among them penicillin, which are never found in the normal blood plasma, but which when artifically introduced into the blood stream are eliminated by the

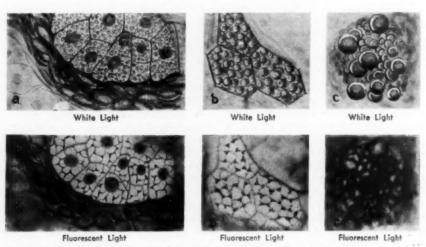
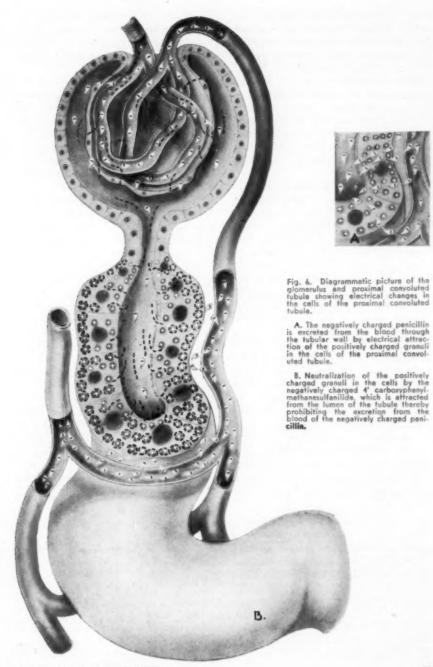


Fig. 5. Drawings of the suprarenal gland showing 2 stages of change efter injury to the body. a. normal, b. beginning damage, c, end stage.



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action of the cells of the proximal convoluted tubules alone or by combined glomerular filtration and tubular secretion. This combined action results in an extraordinarily rapid elimination.

While glomerular action is a filtration depending on the capillary pressure in the glomerular loops, selective reabsorption and tubular secretion is an electrical phenomenon depending on the electrical charge of the various parts of the kidney tubules and that of the individual cells (See figure 6).

The elimination of a group of chemically unrelated substances which have the same electrical charge can be influenced by one substance. If phloridzin, a negatively charged substance, is introduced the positively charged granuli in the proximal convoluted tubules will be saturated and electrically neutralized. Phloridzin by this neutralization inhibits the attraction of the subsequently introduced negatively charged substances and also the selective staining by the negatively charged fluorescent dyes. Phloridzin prevents the reabsorption of glucose, which is negatively charged, and the diabetes caused by phloridzin manifests itself in fluorescence microscopy by the unstainability of the proximal convoluted tubules. On the other hand the neutralization of the avenues of secretion in the proximal convoluted tubules by 4'carboxyphenylmethanesulfonanilide, iodopyracet, para-aminohippuric acid, benzoic acid, or sodium benzoate makes it possible to retard the elimination of penicillin by preventing its attraction and elimination by the proximal convoluted tubules and thereby it is possible to maintain a high plasma level of penicillin for a prolonged period.

The distal convoluted tubules can be influenced by the positively charged mercury salts. By this action the ability of the distal convoluted tubules to reabsorb the positively charged water will be impaired, resulting in increased diuresis. This action manifests itself in the fluorescence microscopy by the unstainability of the distal convoluted tubules.

Fluorescence microscopy enables us to observe the histological manifestation of drug action and the electrocytological interpretation of the findings might give an explanation for the effect of a variety of drugs. Singer and Davis" pointed out seemingly unrelated pathological conditions have in common the reduction of the potential difference between the oppositely charged tissue elements. Two recently introduced groups of substances, which play an increasingly important role in pharmacology, the antihistaminic substances and the steroid hormones of the suprarenal gland, influence the sodium and potassium level of the blood plasma in a manner which indicates that they attain their effect by influencing the potential difference of the oppositely charged tissue elements. By extending our observations to these substances one might open new avenues for therapy and research.

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Robert Latou Dickinson, M.D., F.A.C.S.

The death on November 29, 1950, of Doctor Robert Latou Dickinson, in his ninetieth year, ended a singularly rounded medical career. Its fullness, dynamism and brilliancy rested upon great natural and acquired equipment; distinguished achievement in medicine followed naturally and inevitably as anatomist, gynecologist, educator, assistant chief of medical section, National Council of Defense, Washington, 1917; lieutenant colonel and medical adviser General Staff, Washington, 1918-19; on mission to China for Public Health Service, 1919 and to Near East, 1926; gifted artist, author, sexologist and authority on human fertility and its control.

Doctor Dickinson was one of those of whom the late Doctor William A. White, in his Mechanisms of Character Formation, said, "The tremendous energy distributed by some persons would seem, could it be concentrated, controlled and transmitted, sufficient to light a city." Doctor Dickinson shed light on many cities.

Our own liveliest appreciation relates to Doctor Dickinson as artist; the domain in which he excelled was art; as a pioneer in the field of adequate textbook illustration he set the pace for American creation. His original visual-aid resources in the medical classroom enhanced teaching effectiveness amazingly. He included sculpture in his wide range (witness his work in the Cleveland Health Museum), like his early colleague Professor Alexander J. C. Skene.

What especially stimulated the budding spark of genius in this man? His early education abroad made him a Continental European in a cultural sense, but thereafter he was exposed to a milieu which in his young manhood was probably the stuffiest and most puritanic in the world. It is our belief that it was the reaction of an artist intellectually conditioned in a foreign world of enlightenment and exceptionally endowed by nature, to this bourgeois environment, that resulted in the prolific series of creations and writings that have brought the subject of human sex anatomy and physiology, as well as the large social implications in his presentations, as far to the fore as it has been expedient, or possible, to go at the present time.

In his book, The Single Woman, in Chapter 1, significantly titled 1895, Dickinson himself paints a deadly picture of that period in our history of benightedness: "The Anthony Comstock blue laws had been in existence since 1873. The medical concept of insanity was of an incurable state. The movements for social hygiene and mental hygiene had not come into existence. . . . In these days and with these folkways, sexual feeling could not be admitted, and emotions were in the romantic key."

Things have changed mightily. The subject of a lecture by Doctor William G. Niederland on December 9, 1950, before the Brooklyn Institute of Arts and Sciences, as one of a series on "Psychosexual Problems of the Adult," was as follows: "Psychopathic Personalities in Human Relations: Perverts, Megalomaniacs, Habitual Liars, Delinquents, Addicts, etc." Such a lecture in Brooklyn in pre-Dickinsonian days would have been inconceivable.

So we even have medical art exhibits today in public institutions, like libraries, and not as always before on some medical

society's premises and restricted to professional and privileged circles, without protest against revelations of human sex anatomy by notoriety seekers-an earnest of the fact that such centers have attained cultural adulthood and that the tree of art itself has been allowed to grow to maturity without outraging moral allergies. There was once a day, not so long ago, when prude, puritan, pious exhibitionist and hypocrite would have risen in arms against such desecration of alleged virtues. Sexological literature sponsored by responsible physicians now baffles a censorship that once upon a time harassed Havelock Ellis. This educational field owes much to Dickinson.

Dickinson liquidated many of the sex taboos of unhappily married folk. Such work was of course resisted by some members of the medical profession which itself, after all, represents a cross section of the country's lingering provincialisms and parochialisms which were ingrained before their medical training supervened. That is always the case in any considerable group of people. It is definitely the case with medicine itself, despite its general cultural stature. We are sociologically and educationally responsible, along with the clergy and the lawyers, for the appalling divorce rate stemming from sexual ignorance, stupidity and invincible immaturity.

Today we have the fine attitude toward this matter of better sexual adjustment exemplified by Reich and Nechtow in their Practical Gynecology (Lippincott Company, 1950): "The doctor should not have any condemnation or prejudices concerning sexual behavior, because unless he is tolerant and understanding, he will be unable to use the psychosomatic approach." The entire profession must shed its sexual anachronisms and archaisms and "grow up" to this enlightened point

Our admiration of Dickinson, because of his genius, has been tempered by two factors. His advocacy of euthanasia always chilled us; and in our view, his evangelism for contraception represented a regrettable appeasement of the social Moloch which vetues motherhood in a materialistic climate inimical to such a freedom. His parenthood planning seemed to us largely an indirect compromise with a rotten social order calling for direct action. But who dares grapple with the minotaur?

The power and passion of authentic genius is a radiant thing. A. C. J.



HYPOMETABOLISM

650 Main St.

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CHEVALIER JACKSON

Classical Quotations

There is an indescribable pleasure created by the removal of a foreign body [as from a bronchus]. . . . If someone has said removal would be impossible, there is a criterion of achievement that enhances the pleasure. Greatest of all such pleasures is the feeling that a life has been saved.

> Chevalier Jackson Autobiography, 1938

EDITORIALS

Greetings from Our New Home

Change, growth, life! In November we entered upon a new phase in the history of the MEDICAL TIMES—we moved into our own building in Great Neck. We believe that this safari presages ever-mounting accomplishment in the journalistic field. Our confidence is chiefly based upon the continued support of our medical contributors and editorial colleagues in every quarter of the United States, from which source we derive the zest, spirit

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and energy wherewith to repay dynamically our loyal clientele. The ardent collaboration of our plant and field staffs is another controlling factor in our mood of confidence.

Since its foundation 78 years ago the MEDICAL TIMES has had but four editors—Egbert Guernsey and A. K. Hills (40 years of service); H. Sheridan Baketel (15 years); Arthur G. Jacobson, present incumbent (24 years to date), from which its institutional stability may fairly

ROMAINE PIERSON PUBLISHERS TEXT BOOKS TE

be inferred.

Our earliest years saw the introduction of salicylic acid, daddy of the aspirin Today we have Cortisone and ACTH. This is a rough measure of the distance traveled by medical knowledge and therapy. Today's new stimuli especially challenge and inspire us. The torch of progress must be passed on, if justice is to be done in our pages to the vast onrush of thought and achievement. The Nobel prize winners Hench and Kendall are merely an avant-garde of a new and amazing age. We must continue to fulfill the promise made by the present editor on the MEDICAL TIMES' fiftieth anniversary (1922)-"We must continue to put our readers in debt to us as one of the worthy medical publications. Our standard of excellence must be maintained and our functions properly adjusted to the prevailing needs of knowledge and practice. We must make our medical literature better while entertaining a serious and lofty conception of editorial duties and responsibilities. And, above all, we must not be timid in our discussion of those things that now threaten the morale of the profession and the foundational principles of our art."

We shall, as always, try to adhere to Lewellys Barker's philosophy of medical editing, whose aspects, he insisted, are intellectual, emotional and aesthetic.

While confessing a soft spot in our heart for the general practitioner, it is as a manifestly real organ of the profession as a whole and not of an aloof group of the eminent or great that the MEDICAL TIMES will continue to woo its esteemed clientele.

Christian Repulses Apollyon

Despite unscrupulous campaigns by antivivisectionists popular votes in Baltimore and Los Angeles have recently sustained the aims and methods of medicine (Baltimore 160,264 to 38,445; Los Angeles 357,939 to 261,699; Time, November 20,

1950). These demonstrations show that the profession's efforts to enlighten public opinion in this sphere of rational thought and action have been well worthwhile, leading, in fact, to deliverance from calamity. These local expressions may reasonably be taken to reflect general attitudes, to be depended upon any time, anywhere, provided we continue to stand guard.

Cultural Confusion

On the one hand, behold the atomic bomb, potential annihilator of mankind. On the other hand, behold the virtual conquest of rheumatoid arthritis and a host of allied collagenic ailments by the weapon of Hench and Kendall. In the case of atomic energy, beneficent uses are pigeon-holed; in the case of the Hench-Kendall bazooka, only beneficent uses come into play.

What a contrast in scientific aims! What a bewildered planet! Suffering and annihilation versus alleviation and life; necrophilism versus hygiene.

Thank heaven we are in the camp of the sane and civilized minority, to say which doubtless sounds vain and boastful. The truth is that medicine is merely fulfilling its traditional role in a barbarous environment.

Euthanasia Boomerang

When one looks into the specific cases in which ardent advocates of enthanasia themselves occupy family relationships to those whose miserable condition largely determines the advocates' position on this subject, one sometimes notes unwholesome psychological factors, directly contributing to the aforesaid miserable condition, for which the ardent and impatient advocates are responsible.

In other words, it is to the advocates, in such cases, that euthanasia should be applied, rather than to the unfortunate patients.

Paronychia (Runaround)

Paronychia is a staphylococcus infection or abscess along the edge of the nail near its base. The most common site of this infection is the proximal portion on either side of the nail (Figure 1).

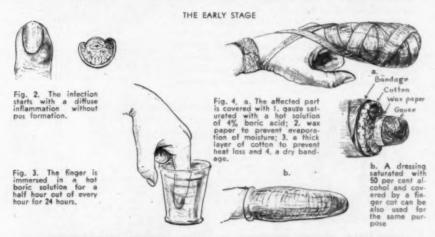
In most cases the infection originates from wounds caused by pulling away or biting off "hangnails." Not infrequently unskillful manicuring is responsible for the infection. As a rule the surrounding tissue builds up a wall of induration and thereby localizes the infection and prohibits its spreading.

The course of the infection has several more or less clearly defined stages, the correct recognition and evaluation of which is essential for effective therapeutic measures.



Fig. 1. Characteristic appearance of the finger end with paronychia.

THE EARLY STAGE of the infection, a diffuse inflammation without pus formation, as shown in figure 2, can be treated with continuous hot boric soaks (Figure 3) or fomentations (Figure 4), which will bring about resolution or the development of a definite localized accumulation of pus. An incision at this stage would be a mistake.



IN THE SECOND STAGE a definite abscess has formed, which lies between the eponychium and the nail, as shown in figure 5. The lifting of the skin edge from the nail with a scalpel will accomplish drainage and immediate relief from pain. This treatment can be carried out without anesthesia. A small rubber dam is placed into the wound. After this procedure a hot boric fomentation is applied for 24 hours to permit discharge of the residual purulent material, as shown in figure 4, or the finger around which a dry dressing is placed can be soaked for one hour with two-hour rest

intervals for 24 hours. The bandage and drain are removed after this period and a dry dressing is applied until the lesion heals.

The material constituting this Department is prepared by Dr. Bernard J. Ficarra, Surgery Editor of Medical Times, and Dr. Edward Singer.



Fig. 5. Pus accumulates, forming a small abscess between the eponychium and the nail.

THE SECOND STAGE

Fig. 6. a, A piece of cotton or steriped is held under the affected finger. The tip of a scalpel is inserted along the edge of the nail at the site of the greatest bulging and the eponychium is lifted up carefully until pus appears. b. The escaped purulent material is wiped off and the nail is separted from the eponychium over the entire extent of the abscess. The overhanging necrotic skin tissue may be cut away, c. A small piece of rubber dam is inserted into the abscess cavity.





Fig. 7. Dry dressing.



THE THIRD STAGE is reached and an incision will be necessary, if the infection has been allowed to progress around the base of the nail as shown in figure 8. This operation should be performed as shown in figure 9.

The surgeon should be cautioned to use a very sharp scalpel as the incision should be made by gliding the edge of the knife over the skin without any appreciable pressure, otherwise purulent material might spray on the surgeon from the abscess. The same after treatment is followed as described above.

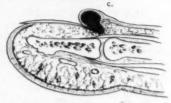


Fig. 8. The untreated infection may extend around the base of the nail to the other side of the nail.

Fig. 10. Avoid these incisions.



Fig. 9. Incision is carried out while holding the infected finger with a cotton pad or steripad. The site of the incision is on the side of the nail, carefully avoiding the underlying matrix and the overlying eponychium, as injury to these parts would cause the development of a malformed nail.



a. This often pictured incision will not drain the side of the base of the nail, which is curved forward.



b. Incision through the matrix will result in the development of a split or ridged nail.

THE FINAL STAGE OCCURS, when a subungual abscess develops (Figure 11). Adequate relief from pain caused by the tension can be obtained only by excising the base of the nail under general anesthesia for which Vinethene or a similar short-acting inhalation anesthetic should be used. If the circumstances do not permit the application of a general anesthetic only then should the operation be performed under nerve block anesthesia, for which 3 to 5 cc. of a 1 to 2 per cent solution of procaine or novocain is used without adrenaline (Figure 12). After completion of the injection a time interval of 5 to 10 minutes is required to produce the analgesia necessary for the operation, which is carried out as illustrated in figure 13. The unaffected parts of the nail should be left in place as these form a protection for the sensitive nail bed. After the operation moist dressings are applied for 24 hours as illustrated in figure 4.



Fig. 11. The infection can burrow be neath the nail to form a subunqual collection of pus with considerable swelling, which causes intense pain.



e. With a 25 gauge needle and a lock type syringe intradermal wheels are raised on each side at the base of the affected finger.



b. Through the wheals the anesthetic solution is injected as the needle advances to the periosteum.





a. Incisions are made through the eponychium along the edge of the neil and carried downward to permit the flapping back of the eponychium to expose the base of the neil.



b. All those parts of the nail which are undermined with pus are entirely removed with scissors.



c. The abscess is packed with petrolatum gauze or a gauze impregnated with penicillin cintment (1,000 to 2,000 units per cc.). Instead of penicillin a 5 to 10 per cent sulfathiazole cintment can also be applied.

HYPERTROPHIC GRANULATIONS occasionally appear at the site of the abscess underneath the eponychium. These should be treated only with a pressure bandage, which will suppress the granulations and healing will take place. (Figure 14).









Fig. 14. Pressure bandage. A gauze pad impregnated with penicillin eintment is placed upon the hypertrophic granulations and a snugly wound dressing fastened with adhesive tape is placed around it.

GYNECOLOGY

HARVEY B. MATTHEWS, M.D., E.A.C.S.°

J. D. Weaver (American Journal of Obstetrics and Gynecology, 60:257, Aug. 1950) states that in a complete gynnecological examination of 1,014 girls at the Austin (Texas) State School, 25.8 per cent showed some inflammatory changes in the genital tract. In 12 cases of vulvovaginitis in which gram-negative diplococci were found in the smears, cultures and fermentation tests showed the organism to be Neisseria sicca, and not the gonococcus. By the examination of the stained smear alone Neisseria sicca cannot be distinguished from the gonococcus. In fermentation tests, the gonococcus ferments glucose alone, and not sucrose, maltose, levulose or mannitol, while Neisseria sicca ferments all these sugars except mannitol. The two organisms can also be distinguished in cultures. In his private practice, the author has seen 3 cases of vulvovaginitis in girls, in which penicillin and the sulfonamides had failed to effect a cure; cultures showed the infecting organism to be Neisseria sicca. Some authors have expressed the opinion that this organism is not a pathogenic organism; however, these studies indicate that it may cause vulvovaginitis, especially in girls. In order to avoid an incorrect diagnosis of gonorrhea in outbreaks of vulvovaginitis in orphanges and schools, it is important to use cultures and fermentation tests in the identification of gram-negative diplococci found in the vaginal smear as these may show the organism to be Neisseria sicca and not the gonococcus.

COMMENT

Vulvovaginitis in young girls is always troublesome. In institutions it is very important from a diagnostic standpoint because of the question of gonorrhea and the necessity for isolation. In private practice it is equally important, and perhaps more so, because the source of the infection may disrupt the family on moral grounds. Dr. Weaver has called attention to the important fact that vulvovaginitis in young girls can be caused by gram-negative intracellular diplococci, which obviously is not gonorrheal. The differential diagnosis is important, particularly in orphanages and schools. Only by culture and fermentation tests can this be accomplished. Smears cannot be depended upon. Remember! Never make a diagnosis of gonorrhea unless you have the facts to prove that your diagnosis is correct.

Hysterography and Hysterosalpingography

R. H. Marshak and associates (Surgery, Gynecology and Obstetrics, 91:182, Aug. 1950) review 2,500 cases in which hysterography or uterosalpingography was done. The best time for either procedure is a week after the cessation of the menstrual period. For hysterography not more than 3 or 4 cc. of the opaque medium is used; when the uterine cavity and the tubes are to be visualized, in sterility cases, larger amounts of the opaque medium must be employed injected under minimum pressure. Various opaque media were used, and the authors conclude that "the perfect contrast media" for uterosalpingography have not yet been found. The water soluble media were found to be very satisfactory, but twentyfour hour film cannot be made with such media: if these media enter the

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tubes and peritoneal cavity they cause some pain; they do not cause damage to the tissues or embolization. Lipiodol is an excellent medium for hysterography; if it is used to visualize the tubes, it may cause fat granulomas or emboli, although these complications were not observed in this series. Hemorrhage occurred in 3 cases; in one of these cases a submucous fibroid and in another an endometrial polyp was found; in the third case the procedure was carried out without clear visualization of the cervix, and at a subsequent operation endometriosis of tubes, ovaries and pelvic floor was found. The most frequent complication in this series was the development of pelvic inflammatory disease, in 7 cases, but in all these cases, there was a history of previous pelvic inflammatory disease. In a large series of cases, it is impossible to do a pregnancy test on every patient before uterosalpingography. In 2 cases, in this series, an early pregnancy was found, but in neither case was the pregnancy interrupted by the procedure. The review of this series indicates that these procedures are safe with proper technique and should be employed when indicated.

COMMENT

The diagnostic value of hysterography and hysterosalpingography is well established. On the other hand, these procedures are not without danger-very real danger-if performed by the untrained physician. Indeed, even when done by "one who know, how" complications may supervene if the proper conditions are not present and a meticulous technic employed. The authors' comments are sane and sound. Your commentator warns "again and again" that these procedures should not be tackled by the inseperienced. Cetastrophic accidents can occur. We know of one.

H.8.M.

Gynecologic Mortality

W. F. Finn (American Journal of Surgery, 79:755, June 1950) reports that there were 140 deaths in 20,617 admissions to the gynecologic service of the New York Hospital from September 1932 to December 31, 1948, a mortality rate of 0.68 per cent. Operation was done in 17,717 of these cases with 75 deaths (0.42 per

cent); 65 deaths occured without a preceding operation. Infection, embolism, cancer and renal failure were the chief immediate causes of death; all but 4 of the 34 deaths due to infection were caused by peritonitis. Cancer was the chief remote cause of death, most frequently cancer of the ovary, of the cervix and of the endometrium. From analysis of the deaths in this series of cases, the author considers that gynecological mortality can be reduced by paying more attention to a history of bowel disturbances in gynecological patients, and considering the possibility of perforation of the bowel and resulting peritonitis or retroperitoneal abscess after x-ray therapy, also by detecting peritonitis in the presence of pelvic masses at operation. Other important factors in reducing gynecologic mortality are the prompt use of "antimicrobial agents" when infection is present or suspected; early rising after operation: prophylactic use of anticoagulants when there is pain in the calf, fever without definite cause, or increased sedimentation rate; early detection and prompt treatment of renal obstruction, pulmonary edema and atelectasis; and careful attention to respiratory or cardiac irregularity during induction of anesthesia or operation. It is also recommended that tubal insufflation should be done only in the first half of the menstrual cycle and that curettage should not be done at the same time; and that elective operations should not be done in cases in which "the surgical risk outweighs the need for surgery."

COMMENT

Mortality rates from surgical operations today are to lowest in the history of surgery. Modernity re-uires that this should be true. A good history, the lowest quires that this should be true. A good history, correct diagnosis, proper pre-operative preparation and good surgical technic is the answer. The author details the gynecologic mortality occurring in 20,617 admissions to the New York Hospital for a sinteen year period. A gross rate of 0,65% and an operative rate (17,117 cases) of 0,42% is certainly outstanding. We can agree with about every statement made by Dr. Finn and hereby congratulate the group at the New York Hospital for their eternal vigilance in giving their patients the benefit of modern treatment. quires H.B.M.

The Conservative Treatment of Salpingitis Complicating Myomata Uteri

H. C. Falk and associates (Annals of Surgery, 132:247 Aug. 1950) report 135 cases in which hysterectomy was done for uterine fibroids at the Harlem Hospital; all these cases were complicated by pelvic inflammatory disease, but bilateral salpingo-oophorectomy was not done. Unilateral salpingo-oophorectomy was done in 85 cases, because of cystic degeneration of the ovary in 71 cases, tubo-ovarian abscess in 8 cases, and hydrosalpinx, Brenner tumor and dermoid tumor in one case each. In 3 other cases a normal ovary was removed, because trauma endangered its blood supply. Only 49 of the 135 patients had previously had children; this "high rate of infertility" is attributed to the salpingitis. Most of the patients were hospitalized for one to three weeks prior to operation and chemotherapy and in some cases antibiotics were employed in the preoperative treatment. There was only one death in the series, an operative mortality of less than l per cent; most patients were discharged on the tenth to the sixteenth day after operation. A follow-up study of 98 of the 135 cases for a period of three and a half years showed 85 per cent clinically cured and 14 per cent improved. In this series of patients, 114 were under forty years of age so that conservation of one or both ovaries was desirable at the time of operation in the majority of cases. Since 1934, bilateral cornual resection has been employed at this hospital as the operation of choice in recurrent salpingitis, as this interrupts "the epithelial continuity" between the cervix and the tubes and prevents reinfection ascending to the tubes. Hysterectomy in the presence of infected tubes has the same effect. With the tube and ovary left in situ, the vascular supply to the ovary is not endangered so that cystic degeneration rarely, if ever, occurs postoperatively:

None of the patients required re-operation because of recurrent tubal infection either at the Harlem Hospital or at any other institution.

COMMENT

Conservative management of pelvic inflammatory disease is always in order—the younger the patient the more conservative. In private practice since the advent of chemotherapy and the antibiotics, surgical treatment of pelvic infection, particularly salpingitis, is rare. Operation is always contraindicated in acute pelvic infection, except for the vacuation of localized collections of pus. Free trainage of pus, while not curative per se, does give welcome relief from pain and fever. Chemotherapy and/or the antibiotics have no appreciable affect once the infection becomes chronic or there is abscess formation. Blood trensfusion is life saving and should be used freely. Dr. Felk and his associates have accomplished excellent results in their management of chronic salpingitis complicating fibroids. We can heartily agree with their treatment with perhaps one exception and that is we do not retain ovaries in such cases after 35 years of age. With modern therapeutics, management of the menopause is usually very satisfactory and we cannot see the rationale of retaining one or both ovaries that have been implicated in a pelvic inflammation, except in the young woman, aged 35 or less. Conservatism for the younger women; radical treatment for those over 35 has given us good results. But we would not quarrel with Dr. Falk and his associates because they choose age 40. Their operative mortality of less than 1% in 135 cases speaks well for their diagnostic and operative skill. That's tops in anybody's clinic.

Brenner Tumor of the Ovary

W. H. Jondahl and associates (American Journal of Obstetrics and Gnyecology, 60:160, July 1950) report that 31 cases of Brenner tumor of the ovary have been observed at the Mayo Clinic in a period of thirty-six years (from Jan. 1, 1911 to Jan. 1, 1947); 11 of these cases have been previously reported, so that this report adds 20 new cases. There were only 2 cases in which the tumor was bilateral in this series; in 24 cases the tumor was of the solid type, and in 7 cases it was located in the wall of a cyst, including one case in which the Brenner tumor was in the wall of a teratoma containing areas of adenocarcinoma and myxosarcoma. Histologically none of the Brenner tumors in this series showed mitotic figures or other evidence of malignancy. The most common clinical findings in these cases was the presence of an abdominal tumor; in the cases in which menometrorrhagia or postmenopausal bleeding occured, some other pathological condition was found

that accounted for these symptoms, and there was no evidence in any case that the Brenner tumor had endocrine activity. In no case could a definite preoperative diagnosis of Brenner tumor be made: the more usual diagnosis was solid or cystic ovarian tumor or pelvi-abdominal tumor. while in some cases the Brenner tumor was only an accidental finding during operation for some other gynecological condition. A number of associated gynecological diseases were found in these cases of Brenner tumor. As Brenner tumors are rarely malignant, simple oophorectomy or salpingo - oophorectomy is the only procedure necessary, unless the presence of other lesions necessitates more extensive surgery. If the Brenner tumor is found to be maligant, bilateral salpingo - oophoretomy with total hysterectomy is indicated. In the patients in this series followed up, there was no evidence of recurrence in any case; the longest duration of life was twenty-five years after operation. In the cases in which the patient had died, no evidence was found that the Brenner tumor was the cause, or a contributing cause, of death.

COMMENT

Brenner tumor of the ovary is rare. However, in late years since the pathology of this tumor has been better understood, meny pathologists, in reviewing their ovarian tumor slides, have changed their diagnosis to Brenner tumor. Even with this correction they are still rare. There is no way of making the diagnosis prooperatively. They are not malignant, although in a few cases a concomitant malignancy of the ovary has been reported. The benignancy of the ovary has been reported. The benignancy of the Brenner tumor is emphasized by most all authorities. This is certainly one condition in which the pathologist is the only fellow who can make the correct diagnosis. The clinician has to "put up with" a diagnosis of overian tumor—cystic or semi-solid or, worse yet, simply pelvic-abdominal tumor—and operate for its removel. More power to the pathologist—we respect him.

OBSTETRICS

HARVEY B. MATTHEWS, M.D., F.A.C.S.*

Cervical Changes in Pregnancy, Labor and the Puerperium

M. Glass and A. B. Rosenthal (American Journal of Obstetrics and Gynecology, 60:353, Aug. 1950) report a study of 51 specimens from the cervix during pregnancy, labor and the puerperium. In 13 specimens obtained at different stages of pregnancy, it was found that in pregnancy there was characteristically a progressive increase in the thickness and cornification of the squamous lining. There also was an increase in both the size and the number of the cervical glands; the amount of interglandular stroma was reduced, and this stroma was edematous; in some cases the glandular hyperplasia and hypertrophy were "extreme." The fibromuscular wall in these specimens consisted chiefly of fibrous connective tissue, with few muscle cells; there was markedly increased vascularity especially in the outer layer. In 23 cervical specimens taken within a few hours after delivery, the characteristic finding was edema and hemorrhage in the interglandular stroma, but in most cases there was no evidence of denudation of the glandular area such as has been described by Stieve. In 15 specimens the squamous lining showed some degree of

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cornification, but in the remainder it was thin. Regression of the changes observed during pregnancy and immediately after delivery in the squamous lining, glands and stroma was evident in the first four days after delivery, but regressive changes in the fibromuscular wall were not marked until after the first week. It was noted in the cervix at term (immediately after delivery) that in some cases there was such marked epithelial proliferation in healing erosions in the endocervix, that the histological findings resembled early carcinoma; care must be taken in differentiating such pseudo-malignant changes from true carcinoma. In 7 patients whose cervical specimens were obtained at autopsy after death from acute toxemia, the squamous lining did not show the thickening and cornification characteristic of normal pregnancy; this is attributed to the decreased estrin levels in the blood in toxemia. The authors suggest that vaginal smears or biopsies from the cervical squamous lining might indicate a diagnosis of toxemia before characteristic symptoms developed.

COMMENT

Comparatively few reports have emanated from the literature dealing with structural changes of the cervix in pregnancy, labor and the puerperium. Hitherto the cervix was simply looked upon as an obstetrical problem—to get the baby through it. The authors of this paper review the literature and bring to our attention the very definite and many changes the tissues of the cervix pass through during pregnancy, labor and the puerperium. These changes are definitely of scientific interest from many angles, mainly from a diagnostic viewpoint. For example, certain cellular changes resemble malignant cells: For example, certain cellular changes resemble malignant cells; certain changes in the squamous cells in the cervix may indicate the presence of foremia of pregnancy before symptoms develop. If this be true see what a big help in treatment this knowledge could fur-nish. Read this article; it will repay you. We need more such studies. H. B. M.

The Management of Cervical Spasm with Dihydroeraptamine Methanesulfonate (DHE-45)

M. J. Baskin and F. W. Crealock (Western Journal of Surgery, Obstetrics and Gynecology, 58:302, June 1950) report the use of dihydroergotamine methanesulfonate (DHE-45) in the delivery of 50 pri-

miparae. Dihydroergotamine is produced by hydrogenation of the natural ergot alkaloid ergotamine and has been found to be less toxic than this natural alkaloid. The DHE-45 solution employed contains 1 mg. dihydroergotamine methanesulfonate per cc. In all the cases in which DHE-45 was given, the patient's pelvis had been found to be normal by x-ray measurements. One cc. of the DHE-45 solution was given by intravenous injection when the cervix was dilated 5 to 6 cm. If the patient had not been given any sedation previously, 50 mg. demerol was given intravenously immediately following the injection of DHE-45. In the cases in which DHE-45 was employed, there had been no progress in dilatation of the cervix for some time. usually for several hours, and after the administration of DHE-45, dilatation was completed promptly; average time twentyfour minutes. The total duration of labor was definitely shortened as compared with a control series of 50 primiparas. The cervix was carefully examined after delivery, and no cervical tears were found in the group given DHE-45; this group also showed neither fetal anoxia, retained placenta, nor postpartum hemorrhage. No undesirable side effects, such as rise in blood pressure, were noted. In multiparas, the authors note, that "even more striking results" have been obtained with DHE-45; in these patients dilatation after the administration of DHE-45 is so rapid that it is given only in the delivery room.

COMMENT

We have always had "waves drugs which hasten the dilatat of popularity" Many of which hasten the dilatation of conservative obstetricians decry the cervix. Many conservative obstetricians decry the general use of such agents. We agree with those who blame the lack of adequate uterine contraction for the non-dilatation of the cervix. Most cervices will dilate normally with physiological labor. Occasionally, of course, cervical dilatation is slow and help is indicated. Apparently dihydroergotamine methanesulfonate (DHE-45) as recommended and used by the authors is a very potent drug for this purpose. We have had no personal experience with DHE-45. We prefer to use "drip" pituitrin intravenously when there is reason to "hurry up" the labor. However, one must always have a good reason for giving any drug to hasten dilatation of the cervix during labor. Be conservativel Be sure you stay with the patient after giving such agents. Accidents do occur in the best regulated services. the

H. B. M.

Advanced Intraligamentary Pregnancy

J. P. Redgwick and associates (Western Journal of Surgery, Obstetrics and Gynecology, 58:424, Aug 1950) report a case of intraligamentary pregnancy of thirty weeks duration; the chief symptom had been recurrent attacks of acute abdominal pain; vaginal bleeding had begun seven days before admission. At operation, the fetal mass lay on the right side of the uterus; the broad ligament on that side could not be demarcated from the mass; the round ligament passed over it; the fetus was macerated. As there was considerable hemorrhage, a supravaginal hysterectomy was done with removal of "as much as possible" of the right ligament containing the fetal sac. In a review of the literature the authors find 70 cases of intraligamentary pregnancy of twentyeight weeks or longer duration reported from 1816 through 1938 by Champion and Tessitore. In the later literature, they find 11 such cases reported in addition to their own case, making a total of 82 cases. In the cases reviewed, as in their own case, there was a history of acute abdominal pain in the early months of the pregnancy. indicating, in their opinion, that intraligamentary pregnancy results from rupture of tubal pregnancy.

COMMENT

Intraligamentary pregnancy must be very rare, It, of course, results from rupture of an ectopic pregnancy. We have seen one case at about 20 weeks duration. The author's one at 30 weeks was quite advanced and apparently had already begun to bleed before operation was performed. The correct diagnosis is not too difficult. Immediate operation, once the diagnosis is made, is the proper treatment. Do not confuse this condition with true abdominal pregnancy where a live baby can be expected. H. B. M.

A Study of Antidiuretic Effect of the Depressant Drugs Used in Eclampsia

W. E. Brown and associates (American Journal of Obstetrics and Gynecology, 60:1, July 1950) report a study of the

effect of depressant drugs (narcotics and hypnotics), used in the treatment of eclampsia, upon diuresis. In experiments on normal pregnant and non-pregnant women it was found that morphine in a dosage of 16 mg. (1/4 gram) given intravenously definitely reduced the urinary output. Further experiments indicated that this reduction in urinary volume was due to a direct action of the drug on the kidney, as the renal plasma flow was reduced and the tubular reabsorption was increased. Previous studies had indicated that Amytal, Avertin and paraldehyde had no antidiuretic effect. Studies by the renal clearance method confirmed the previous findings that none of these hypnotics decreased the urine volume, while Avertin (in a dosage of 100 mg.) was found to increase renal plasma flow and have a slight diuretic effect. As these experiments were carried out on normal pregnant women, further clinical studies on the application of these findings to the treatment of toxemia and eclampsia are necessary before definite conclusions can be reached. Since Avertin and Amytal have been found to be effective in controlling convulsions in eclampsia, however, these studies suggest that their use for this purpose may be preferable to the use of morphine with its antidiuretic effect.

COMMENT

We are no closer today to an understanding of the efiology of eclampsia than we were 40 years ago. It is still a major cause of maternal and fetal morbidity and mortality in many parts of the United States. Since we do not know the cause of the toxemia of pregnancy we have no specific treatment. Dr. Brown and associates have a "good story" on the antidiuretic effect of the depressant drugs used in the treatment of eclampsia. Naturally the most important such drug is morphine. We have always used morphine freely in severe toxemia of pregnancy—always with the idea of helping, in conjunction with other measures, to prevent eclampsia. Perhaps morphine does depress kidney function to a certain degree—more in some cases; less in others, yet it is the best drug we know about in the prevention and/or treatment of eclampsia. We hope Dr. Brown continues these studies, particularly to find out how long these depressant effects last and to what extent these effect can be quarded against. Until more research is done we shall continue the free use of morphine, as we have for the past 35 years, is the management of the severe toxemines of pregnancy, particularly in eclamptic convulsions. lamptic convulsions, H. B. M.

Congenital Thrombocytopenic Purpura

R. D. Epstein and associates (American Journal of Medicine, 9:44, July 1950) report 7 pregnancies in 5 women who had typical purpura hemorrhagica; in one case the first symptoms of purpura occurred only a few months before the patient became pregnant. The platelet count was low in all these cases, the bleeding time was generally prolonged. the clot retraction was poor and the tourniquet test positive in all cases. Three patients had their spleens removed; in one of these cases, the operation was done in the sixth month of pregnancy because of severe epistaxis; in all cases the platelet count rose to normal or above, at least temporarily, and hemorrhagic symptoms were controlled; 6 of the 7 children born had blood platelet counts below 100,000 when delivered or shortly after; 5 children showed purpura. and one of these had melena. But in all these children, the platelet count rose to normal within two years, usually in two to four months after birth and the purpura disappeared. None had severe hemorrhagic symptoms that required blood transfusions. There was, however, "a rough correlation" between the severity of the disease in the mother and in the child. None of the mothers showed any complications during labor or in the puerperium. In a review of the literature, the authors find 39 pregnancies in mothers with purpura hemorrhagica; with the 7 pregnancies reported by them, this makes a total of 46 such pregnancies. Of the children born alive in this series one-half showed congenital thrombocytopenic purpura; but within a few months the platelet count returned to normal. No correlation was found between the presence or absence of the spleen in the mother and the occurrence of the syndrome in the child. It is suggested that congenital thrombocytopenic purpura is due to transfer of some substance, the nature of

which is unknown, across the placental membrane, which depresses platelet formation in the infant.

COMMENT

Thank Heaven! I have never had a personal case of thrombocytopenic purpura in a mother. We saw a case of the late Dr. John O. Polak's in which splenectomy was done at about 30 weeks. The patient died following the operation. Read—and reread—this article. It will repay you many times. It's good!

Primary Rupture of the Upper Membranes in Twin Labor

F. H. Finlaison (Journal of Obstetrics and Gynaecology of the British Empire, 57:423, June 1950) reports 2 cases of delivery of twins in which primary rupture of the upper membranes occurred during labor. In the first case the presenting twin was in vertex presentation, the second, a breach presentation. The presenting twin was delivered spontaneously after artificial rupture of its membranes; the other twin was delivered by podalic version without further loss of liquor. In the second case, the patient was delivered by lower segment cesarean section after rupture of the upper membranes had occurred, because of maternal and fetal distress following prolonged labor: the upper twin was delivered first: the membranes of the lower twin were intact. In both cases the infants were female, binovular twins, and all survived. The author notes that very few cases of spontaneous rupture of the upper membrane in twin deliveries are reported, but he is of the opinion that it may occur more frequently than is generally recognized, and that it may be the cause of malpresentation or distress of the upper twin, or of the interlocking of twins.

COMMENT

Primary rupture of the upper membranes in twin labor must be very rare. We have seen this happen just once in a long and considerable experience. In speaking to several colleagues they assure me that they have never seen a case or perhaps the diagnosis was never made. This accident should be disregarded in the management of twin delivery. When cesaresan section is performed it is easier to deliver the upper baby first, hence, even here the treatment is not altered because of the accident.

OPHTHALMOLOGY

RALPH I. LLOYD, M.D., F.A.C.S.*

Local Antihistaminic Agents in Ophthalmology

Paul Hurwitz (Illinois Medical Journal 98:113, Aug. 1950) reports the use of antihistaminic agents for the local treatment of various allergic ocular diseases and some ocular diseases not due to allergy. Of the 78 cases of allergic origin, 18 were cases of allergic conjunctivitis associated with hay fever; 10 cases of allergic conjunctivitis, blepharitis, iritis and keratitis associated with hypersensitivity to ragweed pollen and other perennial allergens, 24 cases of allergic conjunctivitis, blepharitis and keratitis not of hay fever origin, 5 cases of vernal conjunctivitis and 23 cases of allergic palpebral dermatitis and urticaria. The non-allergic cases included 13 cases of acute and chronic catarrhal conjunctivitis. 5 cases of functional epiphora and 2 cases of ocular asthenopia with intense itching. Of the 100 cases treated, 80 showed definite improvement. Of the 78 patients with allergic conditions, 68 showed definite improvement; 10 of the 13 cases of acute and chronic catarrhal conjunctivitis showed improvement especially in the relief of itching; itching was also relieved in the 2 cases of asthenopia; the 5 patients with epiphora showed no improvement. The best results were obtained with Antistine ophthalmic solution employed for instillation into the eve and Antistine ointment for local application to the palpebral lesions. Histadyl hydrochloride, which was used in solution or as ointment in 7 cases, was found to be less effective than the Antistine preparations.

COMMENT

We are entitled to many more reports of groups of cases treated along these lines before accepting the proposed treatment as a routine.

Clinical and Experimental Observation on the Use of ACTH and Cortisone in Ocular Inflammatory Disease

A. C. Woods (American Journal of Ophthalmology, 33:1325, Sept. 1950) reports cases of iritis, keratitis and uveitis of tuberculous and non-tuberculous origin, and cases of sympathetic ophthalmia in which systemic treatment with cortisone or ACTH resulted in clearing up of the inflammation, reduction of exudates, clearing of the vitreous and relief of the subretinal edema. In a few cases in which cortisone was instilled locally, external inflammation and exudation were rapidly cleared and secondary glaucoma controlled, but there was no evidence of any effect on exudation in the vitreous. the cases in which cortisone or ACTH had the most favorable effect, there was "reason to suspect" an allergic factor in the causation of the inflammatory reaction. In experiments on rabbits, it was found that ACTH and cortisone given systemically and cortisone applied locally block the inflammatory and exudative phases of anaphylactic and allergic reactions. The clinical evidence indicates that this is also true in man, but no evidence was found to indicate that in man they have any effect on "the underlying hypersensi-

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tivity." The best method of treatment of ocular diseases with ACTH and cortisone has not yet been determined; their mode of action is also not known, but the author considers it probable that they act on the mesenchymal tissues "in some way."

COMMENT

The results obtained by these remedies are so impressive in many cases and so disappointing in others that the effort to learn the manner of action and type of case suitable is imperative.

and type of case suitable is imperative.

We must look to the large clinics for leadership and are sure that eventually the problem will be

R. I. L.

Penetration of Chloramphenicol, U. S. P. (Chloromycetin®) into the Eye

I. H. Leopold and associates (Archives of Ophthalmology, 44:22 July 1950) report experiments on rabbits in which it was found that chloramphenicol penetrated the tissues of the normal eye where given systemically or locally. In concentrations that are effective against micro-organisms sensitive to chloramphenicol, this antibiotic caused no damage to the ocular tissues. The authors' clinical experience with chloramphenicol has been limited, but they have found it effective in the treatment of conjunctivitis due to gram-negative organisms and in epidemic kerato-conjunctivitis. On the basis of their studies on penetration of chloramphenicol into the eye, and of their own and others' clinical experience with the use of this antibiotic, the authors conclude that chloramphenicol can be given by mouth in a dosage of 3 to 6 Gm. a day, the initial dose being 3 Gm. For local use in the eye an aqueous solution containing 2.5 mg. per cc. is effective; it can be instilled into the eye, or when deeper penetration is desired, it can be given by tontophoresis or by intraocular injection, without injury to the ocular tissues. For effective treatment of infections with the newer antibiotics, the ophthalmologist, like physicians in other fields, must have connections with "bacteriological facili-

ties," in order to determine not only micro-organism causing the infection, but also the sensitivity of this organism to the various antibiotics. The choice of the drug to be used in ophthalmology must also depend on whether or not effective intra-ocular concentrations can be obtained and maintained without injury to the tissue of the eye. The studies reported and the clinical use of chloramphenicol in systemic infections indicate that chloramphenicol will prove to be a safe and effective drug in many ocular infections, but a wider clinical experience in this field is necessary before definite conclusions can be drawn.

COMMENT

The flood of new remedies with most encouraging prospects of great usefulness has overwhelmed our clinical and laboratory facilities. Wills Eye hospital in Philadelphia is opening a new research laboratory. The laboratories connected with our hospitals are already occupied with routine pathological work and the next step is a separate research laboratory.

Incision and Closure of the Wound in Cataract Operations

F. A. Davis (Archives of Ophthalmology, 44:175, Aug. 1950) presents a comparison of results in 257 cases in which intracapsular extraction was done with the keratome-scissors incision with deep sutures and 202 cases in which the Graefe knife incision was used also with deep sutures; the incidence of some complications in a previous reported series of 500 intracapsular extractions done with the knife incision but with conjunctival sutures only is also noted. This shows that the incidence of complications was higher in cases of keratome-scissors incision than in those with the knife incision, especially the incidence of hemorrhage into the anterior chamber, iridocyclitis, delayed restoration of the chamber and secondary glaucoma. With the keratome-scissors incision, deep sutures are essential; it is also essential with the knife incision when the round pupil technique is used. In the author's experience the best results have been obtained with the use of a conjunctival flap to cover the deep wound completely. While the keratome-scissors incision for cataract extraction is no longer employed as a routine procedure in the author's practice, it is employed in certain cases, especially when the chamber is very shallow.

COMMENT

This article from one of the great eye clinics emphasizes the importance of the conjunctival flap which was introduced by von Graefe many years ago. The early ophthalmologists sought the cause of the complications of eye surgery in the cataract knife and type of incision, They did not have the benefits of antisepsis or local anesthesia. When antiseptic measures and local anesthesia with cocaine were combined the results were graitifying. The next problem was to control or prevent squeezing and the introduction of novocaine and the like to temporarily paralyze the deep fibers of the orbicularis was the answer. The introduction of surves was the next great improvement in cateract surgery. For the time at least, the advantages of the conjunctival flap seem to have been forgotten and every one seems to feel that sutures are a must irrespective of the skill or experience of the operator. One of the complications of sutures is epithelial invasion of the anterior chamber; another is the breaking open of the wound when the sutures are removed. The accent is now on sutures but this reviewer feels that the conjunctival flap must go along with the suture.

Increased Accuracy in Squint Surgery

Paul Tower (Archives of Ophthalmology, 44:395, Sept. 1950) describes a new instrument for squint surgery in which a flat, calibrated sliding bar is attached a right-angled advancement forceps: this calibrated bar is thin and takes up little additional space. With this instrument, after the muscle has been severed at its attachment near the sclera, the amount of resection, as measured from the edge of the jaws of the forceps, is indicated by advancing the sliding bar and fastening it in the desired position by tightening the set screw. Sutures are placed at the distal edge of the cross arm of the sliding bar, and the proximal edge serves as a guide for the line of resection. This instrument does not obscure the operative field, does not interfere with placing the sutures correctly and does not cause damage to the tissues, while providing accurate measurement of the resection.

COMMENT

Correction of strabismus is one of the greatest achievements of eye surgery. Many have tried to correlate the amount of advancement or recession with the number of degrees of deviation corrected. There seem to be too many imponderables to reduce the equation to the simple terms desired. Nevertheless every effort consistently employed will add to the final results for any operator who will go into the details of the many factors involved. Even if he does not improve his statistics, he will be a wiser and better operator.

R. I. L.

Cortical Potential Changes in Amblyopia Ex Anopsia

D. Dyer and E. O. Bierman (American Journal of Ophthalmology, 33:1095, July 1950) report an electro-encephalographic study of 33 cases of amblyopia ex anopsia with strabismus (28 children, 5 adults) and 8 cases of anisometropia without strabismus in children: 5 cases of alternating strabismus, and 4 cases of diplopia in adults. The electro-encephalographic records showed abnormal cortical wave patterns in 24 of the 28 children with amblyopia ex anopsia with strabismus, but in only one of the five adults in this group. Abnormal cortical potentials were also found in 3 of the 8 cases of anisometropia without strabismus, and in one of the 5 cases of alternating strabismus. The 4 adults with diplopia had normal electro-encephalograms. These findings indicate that in children with "suppression amblyopia," there is an active suppression of "the form sense" in the cortex, but that some change occurs as they become adults. Further study is necessary before this theory can be definitely accepted. It is suggested also that on the basis of this theory the abnormal cortical excitation in suppression amblyopia in children may account for the behavior problems of these children.

COMMENT

The attention of the student in ophthalmology has been centered upon the retina as the place where anisometropia operates, as the organ controlling fusion, etc., and as the important factor in squint. Researches of the Swiss school of brain study and others, like Henschen, have demonstrated that there is double cerebral representation as well as double stinal representation as well as double stinal representation.

Researches of the Swiss school of brain study and others, like Henschen, have demonstrated that there is double cerebral representation as well as double retinal representation. The Pulfrich stereo-phenomena with other studies point very strongly to the Gennarian strips in the visual cortex as the place where the two dimensional impressions of each eye are

combined into a single three dimensional image. The work of the writer of this and similar articles by others are valuable contributions to a subject which will occupy the minds of brain anatomists and physiologists for many years to come but to each contributor we will be grateful, indeed.

R. I. L.

High Speed Photography of the Anterior Ocular Segment

A. B. Rizzuti (Archives of Ophthalmology, 43:365, 1950) describes a method of high speed photography of the anterior ocular segment. The essential feature of the photographic apparatus employed is the electrical flash tube developed by Edgerton. Either color film or black and white film can be used for high speed photography. While the flash of light with this apparatus is very bright, it is of such short duration that it causes the patient no discomfort and the afterimage is "inconsequential." This method of photography eliminates the ocular

movements and minimizes the corneal reflex conditions that interfere with photography of the external eye, with other methods. With black and white films photographic enlargements can be made that show the capillaries of the limbus, and aqueous veins and the visible portion of the lens as well as the cornea and the iris.

COMMENT

Color photography of the external eye and the fundus has come into general use as a result of adequate films and control of illumination. The exposure must be faster than 1/10th second to obviate blur. As a matter of practice, the usual exposure is 1/25th of a second. The modification of the exposure for external eye pictures is done by changing the aperture of the diaphragm. The modern synchronizer flashes the light end also opens the shutter in a very satisfactory arrangement but there is always room for improvement and this device will be welcomed by those who take this type of picture. The keeping of records in hospital and private practice is a matter of the last 25 years and the effects upon practice and teaching are immense. We have in photography of the eye another influence which leads to better observation and more exact reporting of results and progress of disease.

R. I. I.

Asks Doctors' Aid in Fighting Communism

In a guest editorial, appearing in a recent issue of the Journal of the American Medical Association, John Edgar Hoover, director of the Federal Bureau of Investigation, asks "the physicians of America, like other citizens," to help protect the nation's internal security.

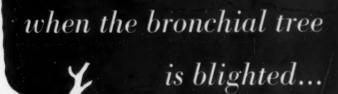
He asks doctors to report immediately to the FBI "any information of this nature which might come into their possession."

"The FBI," he said, "is not interested in opinions or ideas, idle rumor or malicious gossip—only in facts. Like you, as physicians, we want to know the unvarnished facts of the case. To fulfill our responsibilities, we seek to determine all available facts and then forward them without comment or evaluation to the Department of Justice.

"Americans can defeat the Communist

challenge—and in a democratic manner. Witch hunts, hysteria and vigilante actions are repugnant to the democratic tradition. They weaken the majesty of law and provide the Communist agitators with additional talking points. If each person in America would stop and think, learn to 'peel off' the 'outer skin' of Communism, often deceptively painted with glittering promises and glorious utopias, and recognize Communism for what it is—terror and injustice—then America would have no fear.

"The keys of victory must be alertness, eternal vigilance and the maintenance of calmness. A healthy nation, like a healthy body, must receive the unstinting cooperation of all its component parts; if one part fails to carry its share the whole organism is weakened. America, at this critical hour, must remain strong and healthy. This is the task of each and every person."



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New Edition of Stedman

Stedman's Medical Dictionary of words used in medicine with their derivations and pronunciation including dental, veterinary, chemical, botanical, electrical, life insurance and other special terms; anatomical tables of titles in general use, the terms sanctioned by the Basle Anatomical Convention; The new British Anatomical nomenclature: Pharmaceutical preparations official in the U.S. and British pharmacopoeias are contained in the national formulary; and comprehensive lists of synonyms; biographical sketches of the principal figures in the history of medicine. Edited by Norman Burke Taylor, M.D. in collaboration with Allen Ellsworth Taylor, M.A. 17th Edition. Baltimore, Williams & Wilkins Co., [c. 1949]. 8vo. 1361 pages, illustrated. Cloth, \$8.50 with thumb index, \$8.00 without thumb index.

The seventeenth revision of Stedman's Medical Dictionary has the same high qualities as previous editions. The editors have cut out dead wood and revised old definitions, as well as added new words which have come into use since the last revision. As a new feature, short biogra-

phical sketches of principal figures in the history of medicine have been added.

WESLEY DRAPER.

Proctology

Proctology in General Practice. By Comm. (MC) J. Peerman Nesselrod, USNR. Philadelphia, W. B. Saunders Co., [c. 1950]. 8vo. 276 pages, illustrated. Cloth, \$6.00.

The wealth of material for this welcome book was drawn from the author's extensive military and civilian proctologic experience, and represents, therefore, proctology as he practices it. Its scope does not include the abdominal approach to colonic and rectal surgery nor definitive plastic surgery for anorectal anomalies, but the author has covered the anorectal division of proctology with care so that a general knowledge of this specialized field is bound to result from a careful reading of the book.

The opinions expressed, as well as the various diagnostic and surgical procedures, are sound, and generally accepted by proctologists in this country.

There are fifteen chapters which cover the subject in orderly fashion. The 144 drawings and photographs of armamentarium, disease conditions, and procedures are well done and clear, and carry on where the author leaves off. Two of the illustrations are color plates of proctoscopic views of a number of common

-Continued on page 62

1 ST IN THE FIELD! TAR PLUS ANTIHISTAMINE



In many pruritic and allergic skin disorders, the torment of itching is a primary consideration and its alleviation an immediate need. HISTAR'S antihistaminic provides a potent local anesthetic action bringing quick relief of the itching, burning and swelling attending many of these cutaneous disorders.

However, the complete cycle of therapy, as displayed by HISTAR, is fulfilled by the incorporation of tar, universally recognized for its effectiveness in such disorders.

Clinical tests have shown HISTAR to be 72% effective in the improvement, amelioration or disappearance of lesions. In a special study of 54 cases conducted for possible side effects, no evidence of systemic or local

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For prescriptions—all pharmacies stock 2 oz. jars; for dispensing purposes, 1 lb. jars available through your surgical supply dealer.

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conditions such as chronic ulcerative colitis, tuberculous rectal ulcers, venereal lymphogranulomatous rectal stricture, rectal polyps, and rectal carcinomas.

The first chapter, devoted to "Anatomy and Physiology" of the anus, rectum and sigmoid colon, is concise and free from non-essentials. The chapters on "Preoperative Management" and "Postoperative Care" are eminently practical. The last chapter, "Miscellaneous Subjects," is quite interesting, and covers bowel management, enemas, laxatives and mineral oil, suppositories, fecal impaction, anal incontinence, anorectal neuroses, anal warts, preparation for proctoscopy and pilonidal disease.

The format is excellent and the text is presented in clear, concise language and in a manner easy to follow. There is a fine index and the printing is all that could be asked. The reviewer heartily recommends it to anyone who has occasion to refer to a book on the subject.

A. W. MARTIN MARINO

Experimental Surgery

Experimental Surgery, Including Surgical Physiology, By J. Markowitz, M.B.E. 2nd Edition, Baltimore, Williams & Wilkins Co., [c. 1949]. 8vo, 546 pages, illustrated, Cloth, \$7.00.

This new edition should be studied not only by all surgeons but by physicians as well. The foundation experiments on which modern anatomical and physiological surgery has been built will coordinate the studies of the recent graduate and will give older men the reasons for many principles discovered since they received their degrees. It is much easier to comprehend and use these ideas when one sees how they have been discovered.

Chapter VII, on principles of chest surgery, must have been missed in the rewrite as many of the procedures advised have been superseded. In later chapters on the heart, vessels and lungs the more modern concepts appear. There is a tendency to imply that the experimental results will prove as successful in human surgery. Vagotomy, as an example, seems not to have lived up to promise.

WM. H. FIELD.

Oto-Allergy

Allergy in Relation to Otolaryngology. By French K. Hansel, M.D. Panel Discussion, Harold A. Abramson, M.D., Kenneth L. Craft, M.D., Jerome Glaser, M.D., Irving B. Goldman, M.D., et al. An official publication of the American College of Allergists. St. Paul, Bruce Publishing Co., [c. 1949, The Author]. 12mo. 77 pages, illustrated. Cloth, \$2.50.

In this book Dr. French K. Hansel has given a short and concise exposition of the modern concept of Allergy in relation to Rhinology. His cytologic pictures and their evaluation are instructive. Then follows the panel discussion in which the surgeons, allergists and those with the psychosomatic approach give their experiences and their views. It is a very interesting book and should be read by all in the field.

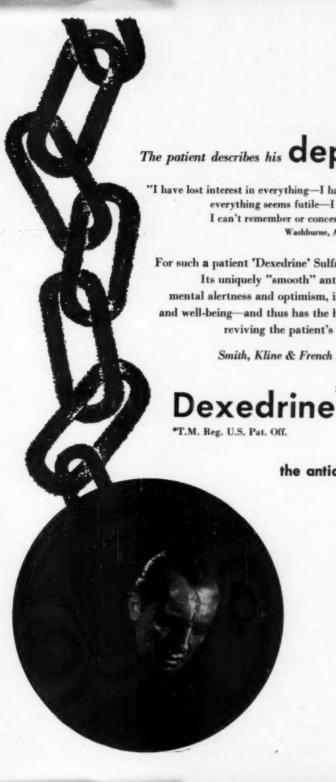
DOROTHEA E. CURNOW

Chest Disease

Differential Diagnosis of Chest Diseases. By Jacob Jesse Singer, M.D. Philadelphia, Lea & Febiger, [c. 1949]. 8vo. 344 pages, illustrated. Cloth, \$7.50.

This book provides us with a masterful presentation of the diagnostic problems arising in diseases of the chest and is a very thorough and up-to-the-minute covering of the subject by one who has had considerable experience in this field. It is, therefore, entitled to respect and study. The illustrations are excellent and the text is unusually lucid and readable. The general practitioner as well as those especially interested in chronic pulmonary diseases will find it a profitable book to explore.

FOSTER MURRAY



The patient describes his depression:

"I have lost interest in everything-I have no ambition any moreeverything seems futile-I feel frustrated and lonely-I can't remember or concentrate-I am all slowed up." Washburne, A.C.: Ann. Int. Med. 32:265, 1950.

For such a patient 'Dexedrine' Sulfate is of unequalled value. Its uniquely "smooth" antidepressant effect restores mental alertness and optimism, induces a feeling of energy and well-being-and thus has the happy effect of once again reviving the patient's interest in life and living.

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MODERN

THERAPEUTICS

Antihistaminic Agents in Ophthalmology

Local application of the antihistaminic drug Antistine was tried in 80 cases of ocular allergic conditions and in 20 cases of ocular conditions of non-allergic origin but showing the same symptoms. The predominant symptoms were ocular itching, tearing, redness, mucous secretion, burning sensation, and photophobia. The conditions of non-allergic origin treated were chronic catarrhal conjunctivitis, epiphora, and ocular asthenopia.

Hurwitz reported in Illinois Med. J. [98 (Aug. 1950)] that symptomatic relief was obtained in 68 of the 80 cases of allergic ocular conditions and in 12 of the 20 cases of non-allergic origin. None of the 5 cases of functional epiphora obtained any relief. In some of the cases pathological conditions improved along with the relief from symptoms. The marked effect upon the itching caused the author to consider the possibility that the itching may be the result of a sensitization of the nerve endings by the elaboration of histaminic end products due to the inflammation or conjunctival irritation. Inactivation of these end products, or their preclusion to the cells by the local action of the antihistaminics may be the action by which the itching was stopped. A 0.5 per cent isotonic, buffered solution with a pH of 6.9, a 0.25 per cent ophthalmic ointment with a petrolatum base and a 3 per cent cream containing Antistine hydrochloride were the preparations employed.

Histadyl hydrochloride in a 0.5 per cent solution and a 0.5 or 1.0 per cent ointment were tried in 7 cases with various ocular conditions. These products

were in an experimental stage and it was felt that buffering the solution and changing the ointment base might improve the results. As the preparations stood the results were not as good as those with Antistine.

Mesantoin in the Treatment of Convulsive Disorders

Methyl-phenyl-ethyl hydantoin (Mesantoin) was administered in reported doses ranging from 0.1 to 0.4 Gm. a day to 54 patients with convulsive seizures, the majority of which were classified as grand mal. Among the 54 patients 42 were considered to have been benefited by the treatment. In all of the patients other anticonvulsants had been ineffective or toxic.

Marsh and Miller, writing in Bull. Los Angeles Neurol. Soc. stated that it was found best to prolong the change-over to Mesantoin therapy over a period of 2 to 4 weeks rather than the 7 to 10 days initially tried. The relative toxicity of Mesantoin was found to be low and only 15 of the series showed signs of toxicity. Of these it was necessary to discontinue treatment with only 7 patients. The authors pointed out, however, that close supervision should be employed whenever Mesantoin is administered in order to avoid unpleasant side effects.

Clinical Evaluation of Methergine

Methergine (d-lysergic acid-dl-hydroxybutylamide-2) was administered to a series of 550 patients in a concentration of 0.2 mg. per cc. A series of 406 patients, to whom was administered ergonovine, acted as controls. In both groups about 80 per cent of the patients were either primigravidas or secundigravidas. The first contraction of the uterus occurred within 2 minutes following the injection of Methergine in 89.63 per cent of the cases

-Continued on page 58a



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Capsules





Capsule form easier to take - Capsule breaks down quickly; unlike tablet, causes no feeling of stickiness in throat. Easier

Smoller dosoge -2 capsules 1 to 3 times daily at first. than drinking gels.

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e-Evaluation of Hydrophilic Properties of Bulk Laxatives, Including the New Agent, Sodium Carboxymethylocillulose, Blythe, Rudolph H., Galessch, John J., and Tut, hill, Harlan L., Scientific Edition, Journal of American Pharmacontical Association, February, 1949.

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SQUIBB

MODERN THERAPEUTICS

-Continued from page 56a

and following the injection of ergonovine in 94.83 per cent. The time from injection to the end of the 3rd stage of labor was within 5 minutes in 87.27 per cent of the patients given Methergine and 80.54 per cent of those given ergonovine. There was no difference of statistical significance in the blood loss between the two groups, according to Schade and Gernand in Am. J. Obst. Gynecol. [59:627 (1950)]. None of the patients experienced undesirable side effects from the Methergine. The authors concluded that the drug is a safe, potent oxytocic drug that corresponds in several details of its action with ergonovine.

Effect of Desoxycorticosterone Acetate and Vitamin C in Rheumatoid Arthritis

There have been many and conflicting reports on the effectiveness of adrenal hormones on the course of rheumatic diseases. Mettior, Gordan, Rinehart, Plumhof, Ellenhorn, and McBride contributed in Bull. Univ. Calif. Med. Cent. [1:337 (Jan. 1950)] the results they obtained in the treatment of a group of 25 patients with rheumatoid arthritis and I patient with rheumatoid arthritis combined with disseminated lupus ervthematosus. Treatment was composed of 5 mg. of desoxycorticosterone acetate given intramuscularly followed by an immediate intravenous injection of 1 Gm. of sodium ascorbate. The schedule of treatment was every 8 hours for several days for 3 patients, daily injections for 2 patients, weekly injections for 14 patients, and twice weekly injections for the remaining patients.

In all of the patients there was a prompt lessening of pain and tenderness and an increased range of motion in the involved joints. The authors emphasized that the optimum dosage schedule has not been determined but that in their experience there seemed to be no advantage to injections more frequently than twice weekly.

The authors also emphasized the need for careful observation of weight, blood pressure, and of the presence or absence of edema. Salt retention and mild edema occurred in some of the patients given daily or more frequent doses of the hormone.

Viomycin Experimentally Successful Against Tubercular Organisms

A new antibiotic, Viomycin, has shown ability to combat experimental tuberculosis in test animals and can be used on human beings over a prolonged period, according to a series of reports presented before the National Tuberculosis Assoc. meeting in Washington, D. C. in April, 1950. Dr. G. Hobby and Dr. W. Steenken reported studies in mice and guinea pigs and concluded that the antibiotic can suppress tuberculosis to a considerable degree in these animals. Dr. W. McDermott and Dr. R. Tompsett stated that the antibiotic had been given a limited trial in human beings but that no real determination of therapeutic value in man had as yet been made. They stated that the most promising aspect of the antibiotics action was that it seems to be active against tuberculosis organisms which have become resistant to streptomycin.

Use of Dramamine in Motion Sickness

Dramamine (B-benzohydryloxy-N, N-dimethylethylamine 8-chlorotheophyllinate) was studied in a group of widely separated trials in the U. S. Navy, involving 893 men. The drug was reported by Shaw in *Military Surg.* [106:441 (June 1950)] to be very effective in doses of 50 or 100 mg. in the prevention of sea-sickness on a 90-minute trip on landing craft

-Continued on following page

Multiple Vitamin Therapy

"... Patients fare much better when [the deficiencies] are treated simultaneously... Convalescence is delayed when one gives only one vitamin at a time..." (Spies & Butt in Duncan, G. G.: Diseases of Metabolism, ed. 2, Philadelphia, Saunders, 1947, p. 504.)

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SQUIBB

MODERN THERAPEUTICS

-Continued from preceding page



for Coughs...

in acute and chronic bronchitis and paroxysms of bronchial asthma . . . whooping cough, dry catarrhal coughs and smoker's cough—

PERTUSSIN

with no undesirable side effects for the patient, helps Nature relieve coughs when not due to organic disease.

Its active ingredient, Extract of Thyme (Taeschner Process), acts as an expectorant and antispasmodic. It increases natural secretions to soothe dry, irritated membranes. It may be prescribed for children and adults. Pleasant to take.

Trial packages on request.

SEECK & KADE, INC. New York 13, N. Y. and in a group of susceptible subjects on an ocean crossing. However, it was reported to be no more effective than a placebo on 3 Coast Guard ships. The drug also was markedly beneficial in curing sea-sickness in doses of 100 mg. Benadryl was also effective in doses of 50 mg. but both drugs caused drowsiness in about 25 per cent of the cases.

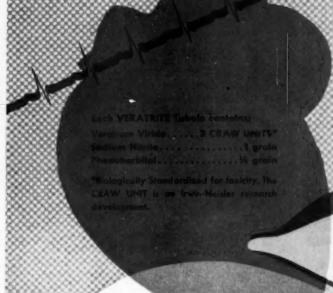
In the treatment and prevention of airsickness Dramamine was as effective as scopolamine and, in one group, there were fewer side relapses than after scopolamine. There was no evidence of deleterious effect on marksmanship and no evidence of toxicity, even after repeated dosing. Mild headache, drowsiness and dizziness were questionable reactions. When favorable action occurred it was prompt and lasted to 3 to 4½ hours following a single dose.

Sulfonamides in the Treatment of Bacillary Dysentery

Eleven of 27 children with Shigella sonnei dysentery were cured as indicated by negative smears on the 4th to 7th day. Treatment consisted of 0.2 Gm. of sulfadiazine per Kg. per day plus double that amount of sodium bicarbonate. Of 28 receiving 1.5 Gm. of phthalylsulfacetimide who were 2 to 6 years old, 2 Gm. for those 6 to 10 years old, and 4 Gm. for those over 10 years old, 11 were cured. A mixture of equal parts of sulfadiazine, sulfamerazine, and sulfacetimide given in doses of 0.2 Gm. per Kg. per day produced a cure in 20 of 24 children in one course of treatment.

Lehr, Luetters, Capute, Abramson, and Slobody, reporting before the April 1950 meeting of the Am. Soc. Pharmacol. Exptl. Therap. stated that the superiority of this mixture was not explained by the fact that it produced higher blood levels

-Continued on page 62a





In Mild and Moderate Hypertension, a marked sense of well-being is provided by the routine administration of Tabules Veratrite. Pronounced relief of headache, dizziness, fatigue and nervous irritability is accompanied with a reduction in blood pressure. Veratrite lessens peripheral resistance without compromise of circulation.

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Each tablet contains:

Dehydrated Prune Concentrate

Methylcellulose (6 gr.) (0.39 gm.)

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ADULT DOSAGE: 3 or more toblets with normal elimination is established; then

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MODERN THERAPEUTICS

-Continued from page 60a

than sulfadiazine, since phthalylsulfacetimide produced as good results as sulfadiazine and was not absorbed to any appreciable extent.

Severe Hypertension Treated with Hexamethonium Bromide

Eight cases of severe hypertension with papilloedema were treated orally with hexamethonium bromide. An initial dose of 0.25 Gm. was given in about 10 cc. of water. This dose was repeated twice on the first day and 3 times on each of the next 2 days. Then the dose was increased to 0.5 Gm. 3 times a day. Similar increments were made until 0.5 Gm. was being given 4 to 6 times a day by the tenth day of treatment. Large initial doses produced circulatory collapse in 2 patients but the low initial dose with the increments described circumvented that difficulty.

Campbell and Robertson presented the results of this study in the Brit. Med J. [No. 4683:804 (Oct. 7. 1950)]. They stated that the blood pressure levels were maintained at normal or at the level determined to be optimum for the patient on the dosage described. Headache, was abolished, papilloedema was reduced, and vision was improved in every case. Therapy was withdrawn in 3 patients without an immediate rise in blood pressure. One of these 3 patients had maintained normal levels for a period of 8 weeks.

Side effects of blurring of vision, dry mouth, nausea and heartburn, and constipation were encountered in every patient but these effects had subsided by the end of 2 weeks of treatment. Any significant increase in dose brought a recurrence of these side effects but they again soon disappeared.

-Continued on page 64a

MEDICAL TIMES

practical ideals in diabetes





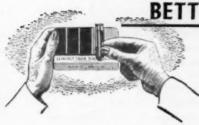
"The ideal detection center is in the private physician's office." This approach to widespread early diagnosis of diabetes can be practical when every routine examination of every patient includes urine-sugar analysis. Routine analysis, in turn, is more practical for the physician who uses Clinitest (Brand) Reagent Tablets. The test is simple, rapid and self-contained (no external heating). Results are known at once

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for urine-sugar analysis

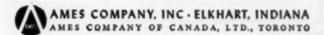
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"Generally, only the well controlled diabetic patient may expect to live to normal expectancy and without premature arterial degeneration." Here too, practicality recommends Clinitest. The Clinitest (Brand) Urine-sugar Analysis Set (a compact pocket unit) enables the patient, under the physician's guidance, to make regular checkups simply, accurately and conveniently. This is a practical guarantee of the patient's cooperation without which adequate control by the doctor is hardly feasible.

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Bibliography: (1) Wilkerson, H. L. C.: New York State J. Med. 49:2945 (Dec. 15) 1949. (2) Sweeney, J. S.: Texas State J. Med. 45:623 (Sept.) 1949.

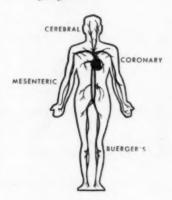


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Symptom-free periods of 10 years and longer.

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Extraordinary and challenging recoveries made when other therapy failed.

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MODERN THERAPEUTICS

-Continued from page 62s

A

Artane in the Treatment of Parkinsonism

Marked immediate improvement was observed in 11 of 12 patients with idiopathic, postencephalitic or senile parkinsonism who were given 2.5 mg. of Artane (α-cyclohexyl - α - phenyl-1-piperidinepropanol). This initial dose was increased daily by 2.5 mg. until 12.5 mg. was being given each day in 5 divided doses. Ellenbogen, writing in *Lancet* [258:1034 (1950)], stated that the 1 failure was a 74 year-old woman with senile parkinsonism of 2 years duration.

Doses of more than 12.5 mg. a day had no increased benefit and caused the development of side effects such as dizziness, blured vision, headache and depression. Side effects appeared in 3 patients who were receiving 12.5 mg. a day but these were eliminated by controlling the dose at a lower level.

Sulfamylon in the Treatment of Vaginal Discharge

Chronic nonspecific vaginal discharge was treated in 5 patients with a 5 per cent solution of Sulfamylon hydrochloride (\$\prec{\pi}\cdot\ \arm \text{amino}\ \cdot\ \perp \text{-toluene-sulfonamide}\ \text{hydrochloride}\) containing 20,000 units of dihydro-steptomycin. The solution was applied by tampon for 48 hours at each treatment.

Moloy stated, in N. Y. State J. Med. [50:992 (1950)], that there was a cessation of discharge in some patients and a reduction in the degree of cervical erosion and hypertrophy. The vaginal smear before treatment showed large numbers of small Gram-negative or Gram-positive organisms but no Doderlein-like bacilli. Following treatment the smears contained predominantly Doderlein-like bacilli. Con-

-Continued on page 66s

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- Felsol is well known and prescribed by physicians in nearly every civilized country . . .
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MODERN THERAPEUTICS

-Continued from page 64a

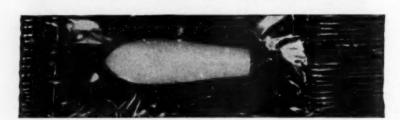
ception occurred in some of the previously sterile patients who used the treatment at the time of ovulation.

Use of Alpha Toluyl Urea in Epilepsy

Alpha toluyl urea (Phenurone) was administered to patients with recurrent convulsive disorder in doses of 0.5 to 6 Gm. a day for 2 weeks to 10 months without discontinuing other anticonvulsant therapy. There was an average improvement of 59.5 per cent in 31 patients over the best prior treatment. The average improvement was 53.8 per cent in 21 cases of grand mal, 33.3 per cent in 3 cases of petit mal, and 66.3 percent in 24 cases of psychomotor seizure. Phenurone appeared to be responsible for most of

the improvement in the psychomotor seizures but some of the improvement in the petit mal seizures could be traced to other drugs. The maximum improvement occurred within 2 months of therapy and on doses of 2 Gm. a day or less. Recurrences of seizures usually occurred within 1 to 3 days of the withdrawal of Phenurone.

Little and McBryde reported in Am. J. Med. Sci. [219:494 (1950)] that toxic symptoms were evident in 15 patients but that they usually subsided when the daily dose was reduced to 1.5 to 1 Gm., although the drug had to be discontinued in 5 patients after 2 weeks to 8 months of treatment. The toxic symptoms manifested themselves by action on the central nervous system in the form of drowsiness, nervousness, excitement, visual disturbances, psychosis, headache and insomnia. One additional patient developed severe leukopenia which disappeared upon the



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Convenient: Individually packed. No refrigeration necessary.

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Vitamin D (Irradiated Ergosterol) 400 U.S.P. Units	Nia
Vitamin B ₁ (Thiamine Hydrochloride). 2 mg.	Cal

Vitamin B ₂ (Riboflavin)	2	mg.
Vitamin B ₆ (Pyridoxine Hydrochloride)	0.5	mg.
Vitamin C (Ascorbic Acid)	37.5	mg.
Niacinamide	20.0	mg.
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*Equivalent to 15 grains Dicalcium Phosphate Dihydrate

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MODERN THERAPEUTICS

-Continued from page 66a

withdrawal of Phenurone and the administration of penicillin.

Antigenic Activity of Dry Glucose BCG Vaccine

A lyophilized vaccine prepared so that the original suspension contained 20 mg. of BCG suspension per cc. of 50 per cent glucose was found to maintain its virility for a year or more when stored at 2 to 4° C., as compared with an optimum antigenic life of but 10 days for the fresh liquid vaccine. The short life of the fresh vaccine dose not allow proper time for desirable tests for purity, harmlessness, and antigenic potency to be performed before it is used in human beings.

The lyophilized vaccine was found by Birkhaug, as reported in the Am. J. Pub. Health [40:545 (May 1950)], to contain less living elements than the fresh vaccine. This was evidenced by a lower antigenicity. The author reported that it was felt that the difference was quantitative rather than qualitative for the surviving organisms retained their original cultural, morphological and biological characteristics. Studies were in progress to attempt to prove the belief that identical antigenic results can be obtained with the dry vaccine if the dosage of living elements is adjusted to correspond to the dosage in the fresh liquid vaccine. The usual intracutaneous dose is 1,750,000 to 3,500,000 living elements. Such a dose produces a tuberculin positive reaction within 8 weeks in about 95 per cent of children and adults vaccinated, which lasts for a year or so. However, the allergy produced by this one injection lasts for about 5 years. This fact brings in the problem that the adjusted dosage of dry vaccine will contain a large amount of killed elements and the allergenic impact will thus be increased.



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 Abramson, H.: "Fotal Baric Acid Paisoning in a Newborn Infant," Pediatrics 4:719-22, 1949.

 Ross, C. A. & Conway, J. F.: "The Dangers of Boric Acid," American Journal of Surgery, 60:386-395, 1943.

 Lictman, A. L., et al: "Tolc Granulomo," Surg. Gyn. & Obst. 83:531-546, 1946.

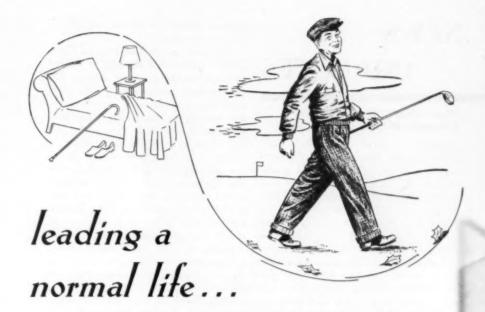
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NEWS

AND NOTES

"Tele-Clinic;" Motion Picture Chronicle of Medical Meetings

First in a series of "Tele-Clinics,*" motion picture reports on medical meetings of national and international significance to the medical profession, has been produced by Wyeth Incorporated, Philadelphia pharmaceutical firm.

The first "Tele-Clinic," released throughout the country recently, features highlights of the Fourth General Assembly of the world Medical Association which convened in New York. The production is a 35-minute, 16 mm, black-and-white sound film which spotlights and reviews the important conferences and

business sessions of the five day World Medical Assembly.

Fifty prints of the first issue of "Tele-Clinic" will be made available to medical societies, hospitals, nurses groups, and other medical organizations by the pharmaceutical concern as a service to the profession. It is estimated that over 300,000 medical people in the country will have access to a showing of the film.

One of the highlights of the film is the adoption of the new medical oath, The Declaration of Geneva, by delegates to the Assembly representing more than a half million physicians. The Declaration embodies a new code of ethics for the profession presented at the London Assembly in 1949. Dr. Louis H. Bauer, secretary-general of the association, presents the Declaration of Geneva for "Tele-Clinic."

Abstracts of the four scientific papers presented to the delegates have been in-

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-Continued on page 72a

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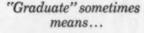
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NEWS AND NOTES

-Continued from page 70a

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corporated in the film as another highpoint in the five-day session. Alfred Blalock, M.D., surgeon-in-chief, Johns Hopkins Hospital, Baltimore, reports on Advances in Cardiac Surgery. Louis K. Diamond, M. D., Boston, medical director of blood banks, American National Red Cross, discusses Therapeutic Uses of Blood Derivatives. The Stress and Adaptation Syndrome is the title of the paper presented by Hans Selve, M. D., professor and director of the Institute of Medicine and Experimental Surgery, University of Montreal. Dr. Albert F. R. Andersen, Brooklyn, clinical professor of medicine, State University of New York, State University Medical Center at New York City, College of Medicine, presents a review of Gastroenterology.

Dr. Elmer L. Henderson, president of the World Medical Association, and also president of the American Medical Association, delivered his inaugural address before the assembly. Portions of the address have been recorded for "Tele-Clinic."

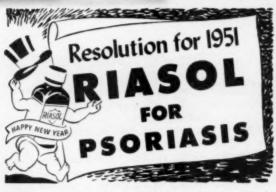
A schedule of films to be produced during 1951 is now being prepared. It is planned to film many of the major medical meetings in cooperation with the various medical societies and to distribute these films periodically.

Calls Family Doctor Guide in Old Age

With the problems of aging increased as a result of the ever-lengthening life span of man, the family doctor is in a position to guide older patients "into the green pastures of old age," in the opinion of a Kansas City (Mo.) surgeon.

Writing in a recent issue of the Journal of the American Medical Association, Dr. Milton Buford Casebolt said the role of

-Continued on page 74a



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NEWS AND NOTES

-Continued from page 72a

the general practitioner is "that of family counselor, skilled in the handling of emergencies in the home and a kindly guide to lead his patients to the achievements of ripe, mature old age."

Dr. Casebolt served as chairman of the Section on General Practice at the annual meeting of the American Medical Association in San Francisco last June.

More persons are reaching old age than ever before," he pointed out. "In the last 50 years a generation has been added to the life span. Prior to 1900 life expectancy was about 40 years; in 1950 the expectancy figures are approaching 70 years.

"Diseases of the aged offer a challenge to the general practitioner. He must know more about the disorders of old age and

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the corrective measures to cushion the aging process in the human body.

"The process of guidance of persons into ripe old age involves rational living, mental maturing and the acceptance of anatomic and pathologic changes in the human body.

"The physician must learn more about the elderly patient who comes to his door. He must offer constructive medicine to the aged. A number of avenues are available in the approach to the problem.

"They are: (1) continued research in the diseases and disorders of the person over 50; (2) education of the geriatric [aged] patient; (3) environment control, and (4) individual guidance.

"The medical aspects involve: (1) periodic health inventory; (2) individual guidance by the family physician; (3) correction of nutritional and glandular deficiencies, and (4) transition from

-Continued on page 76a

4

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NEWS AND NOTES

-Continued from page 74a

active, agressive middle age to a more quiet and serene old age, an aspect that must be well understood by the doctor and the patient. The family physician must furnish the technic and be the traffic manager or director."

He pointed out that the family doctor finds himself many times in the field of mental and nervous disorders. He sees the patient in the beginning of psychotic changes—"the personality deviations at this stage."

"Fully one third of the persons who come to my attention are suffering from anxiety complexes, worry, apprehension and fear." he said.

"There are three approaches to the problem.

"First, there is no happy solution. Resignation to the inevitable must be instilled in the mind of the sick person. Here the physician must call for courage and lean heavily on the field of religion.

"Second, the situation involves others than the person who is ill. By conferring with interested parties adjustments can be made to solve the problem.

"Third, this group of facts involves the individual for whom, by alteration of his or her mental attitudes, values can be created on which the patient can build a new emotional bridge over which to cross the chasm of despair and confusion into the sunshine of cheerfulness, hope and faith."

Cortisone Side Effects Reduced by Smaller Dosages, Report Shows

The development of a dosage of cortisone acetate to maintain improvement in cases of rheumatoid arthritis with a minimum occurrence of undesirable side effects is reported in a recent issue of the Journal of the American Medical Association.

-Continued on page 78a



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 Effect of Buffering Agents on Absorption of Acetylsolicylic Acid J. Am. Pharm. A., Sc. Ed. 39:21, Jan. 1960.

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NEWS AND NOTES

-Continued from page 76a

Cortisone is not a cure for the disease, but its administration reverses crippling results. Its continued use is necessary in order to prevent the return of the pain and deformities which mark rheumatoid arthritis. The problem of physicians using the drug has been to prevent complications in side effects.

A report on the treatment of 42 patients is made by Dr. Edward W. Boland and Dr. Nathan E. Headley of Los Angeles. Based on preliminary studies, they said it appears that some severe cases and most less severe cases may be kept under adequate clinical control for long periods, and with relative safety, with smaller maintenance doses ranging from 32 to 65 mg. a day provided larger doses to suppress the disease are used initially.

"Comparatively few unfavorable reactions have developed when these small doses have been used continuously for as long as six months," they reported. "So far all adverse effects have been temporary, disappearing on hormone withdrawal or lowering of the dosage."

However, they added:

"Only time and further experience will determine the full therapeutic possibilities of cortisone for rheumatoid arthritis. Explorations of its potentialities as a treatment agent are greatly influenced by one fact: The hormone suppresses rheumatic activity but does not cure the underlying disease. Thus, it appears that if antirheumatic effects are to be sustained, cortisone must be given continuously.

"The question as to whether the hormone can be administered safely and effectively for extended periods of many months or years will not be answered positively until there has accumulated greater clinical experience in relation to dosage and methods of administration,

-Continued on page 80a



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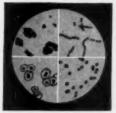
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NEWS AND NOTES

-Continued from page 78a

greater knowledge regarding its physiologic activities and more information as to the consequences of its prolonged or repeated use."

Medical Schools Set Enrollment Record; More Doctors Graduated

The outlook for graduation of more doctors to safeguard the health of the American people is better than it has ever been.

This is brought out in the annual report of the American Medical Association's Council on Medical Education and Hospitals, published in a recent issue of the association's *Journal*.

All records for enrollment in approved medical schools in the United States were broken in the past year, Dr. Donald G. Anderson, secretary of the council, and his assistant, Mrs. Anne Tipner, both of Chicago, said.

The total enrollment in the 72 medical and seven basic science schools for the academic year 1949-1950 was 25,103. This represents an increase of 1,433 students, or 6 per cent, over the preceding year. The latest total is double the enrollment in 1910 (12,530), about 18 per cent higher than 10 years ago, and even larger than during the years of World War II, when extra classes were enrolled in all medical schools on an accelerated program.

From July 1, 1949, to June 30, 1950, 5,553 physicians were graduated from approved medical schools in the U. S., an increase of 459 over the preceding year. This is the largest number graduating from approved medical schools in the nation in one year except for the years 1946 and 1947, when several schools at the con-

-Continued on page 82a

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Archives of Dermatology and Syphilology, February, 1949: 243-245

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NEWS AND NOTES

-Continued from page 80a

clusion of their wartime program graduated more than one class during a 12 months' period.

On the basis of enrollments in the senior class for 1950-1951, the medical schools of the U. S. have estimated that they will have slightly more than 6,000 graduates during the coming year.

The freshman class for the first time exceeded 7,000 students during 1949-1950. The actual number, 7,042, represented an increase of 354, or 5.3 per cent, over the preceding year and an increase of 1,026, or 17 per cent, over the average size of the freshman class in the 10 years preceding World War II.

"The freshman class that will enter medical school this fall will be even larger," Dr. Anderson said. "On the basis of the record of the past year, the new schools that are being organized and the expansion of existing schools that is under way, it now seems likely that within the next few years the freshman class will number close to 7.500 students."

Schools with the largest number of graduates during 1949-1950 were the University of Illinois College of Medicine, Chicago, 161; Jefferson Medical College of Philadelphia, 152; the University of Tennessee College of Medicine, Memphis, 143; Harvard Medical School, Boston, 133; and Northwestern University Medical School, Chicago, 131.

The report said that the budgets of the medical schools and basic science schools for the 1950-1951 fiscal year total about \$67,500,000, representing an increase of about 42 per cent in the last four years. It also said that figures of the cost of new construction, completed, started or authorized during the last year, were available for only one half of the projects reported and the total cost of these was more than \$100,000,000.

Women totaled 1,806, or 7.2 per cent, of the medical students in this country, compared to 2,109, or 8.9 per cent, in the preceding year. The percentage of veterans enrolled in the medical schools and schools of basic medical sciences in the U. S. during 1949-1950 was 65.9 per cent, which is almost identical with the figure 65.8 per cent for the preceding year.

Polls taken in 19 medical schools during the past year reveal that the percentage of students planning to enter general practice has increased from 36 to 47 per cent in the last three years. The number planning to specialize has decreased from 36 to 31 per cent. Other students polled in both periods still had to make a decision.

The problem of formulating a sound program for medical education in the event of another war has been under study by the Association of American Medical Colleges and the A.M.A. Council on Medical Education and Hospitals since the end of World War II, Dr. Anderson said. He added:

"Two days after the invasion of South Korea, the Executive Council of the Association of American Medical Colleges and the A.M.A. Council on Medical Education and Hospitals formed a joint committee on medical education in time of national emergency to represent both organizations in discussions with representatives of government agencies and other groups on all problems relating to medical education during the current crisis.

"This committee has been engaged since June in drafting for submission at an early date to the appropriate government agencies recommendations with respect to the conduct of medical education, including premedical and graduate medical education.

"It is too early to determine whether

-Continued on following page



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NEWS AND NOTES

-Continued from preceding page

drastic changes in premedical education, the organization of the medical curriculum and the training of interns and residents comparable to those put into force during World War II will be sought or whether attempts will be made to place physically qualified medical students on an active duty status in the armed forces.

"It does seem clear that without further delay medical schools will want to review their curriculums to determine how increased emphasis can appropriately be placed on such subjects as military medicine, public health and civilian emergency relief, including the prevention and treatment of casualties from atomic explosions. Planning for dispersal and evacuation of medical schools in the event of bombing of American cities is another topic to which the medical schools will undoubtedly address themselves in the months ahead."

U. S. Maternal Death Rate Establishes New Low Record

For the first time in history, the maternal death rate for a large nation has been pushed slightly below the apparently irreducible minimum of one per 1,000 live births, according to a recent issue of the Journal of the American Medical Association.

This record was set in 1949 by the United States, based on preliminary reports, said the Journal. When the 1949 rates for Sweden, Norway, Denmark, the Netherlands and New Zealand become available, one or more of these small countries with a homogeneous population may join the select circle.

H

The new record, it was pointed out, compares with 1.2 maternal deaths per 1,000 live births in 1948 and with 6.2 in 1933. On that basis, the Journal concluded that "childbirth has been made quite safe."

In 1949 there were 30 states with rates less than 1.0, two at exactly that level and only 17 above.

"The fact that the chances of an expectant mother surviving the diseases of pregnancy, childbirth and the puerperium [confinement period] are now better than 999 out of 1,000 is truly a story of human and social progress," said the Journal. "An examination of the rates for the different states indicates areas in which further improvement can be expected, but it is clear that maternal mortality is no longer a nationwide problem."

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